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Science

Public Health



Cosmic-Ray Laboratory Atop Mt. Evans

(See page 498)

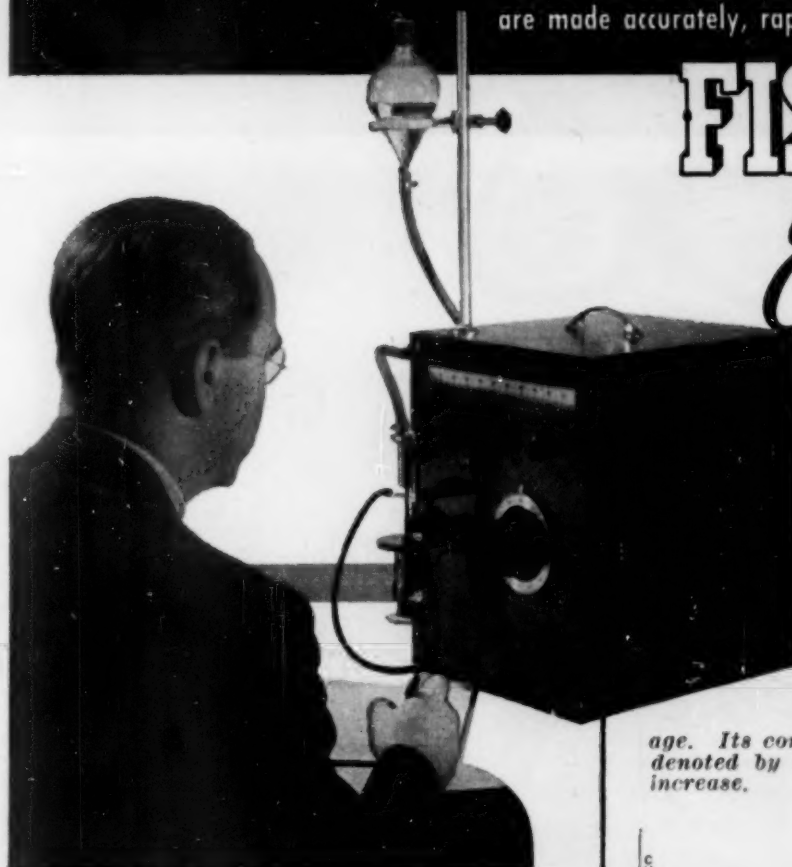
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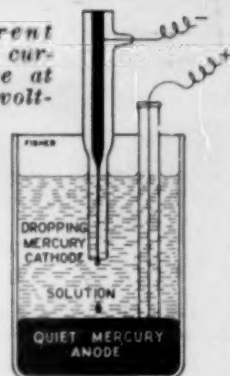
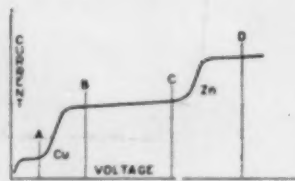
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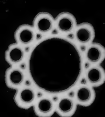
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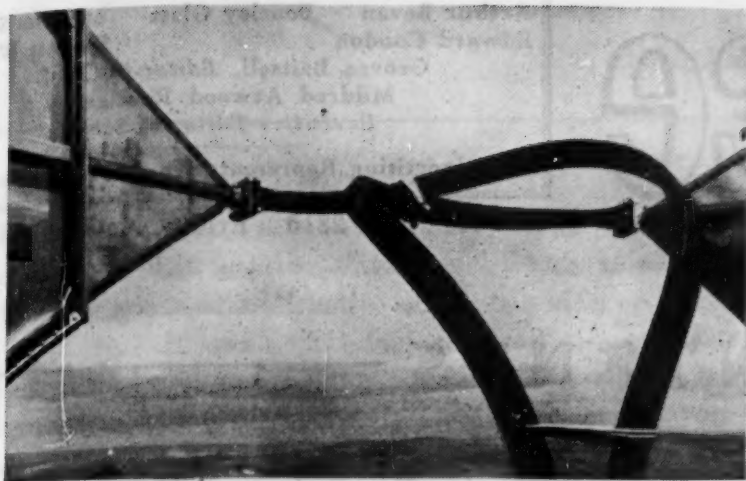
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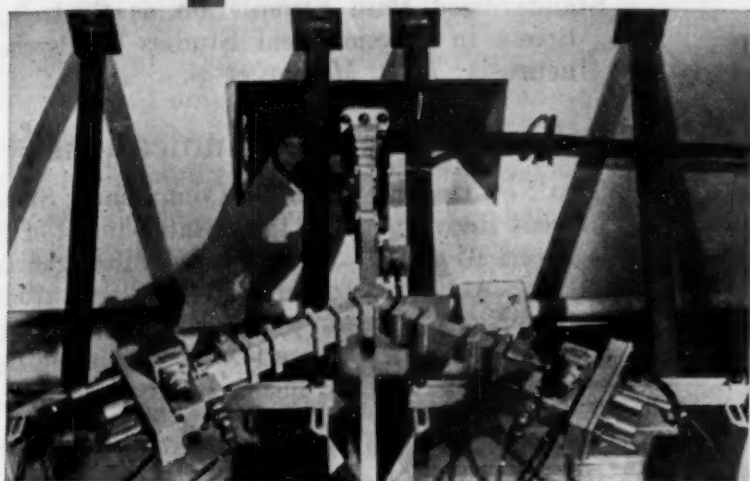
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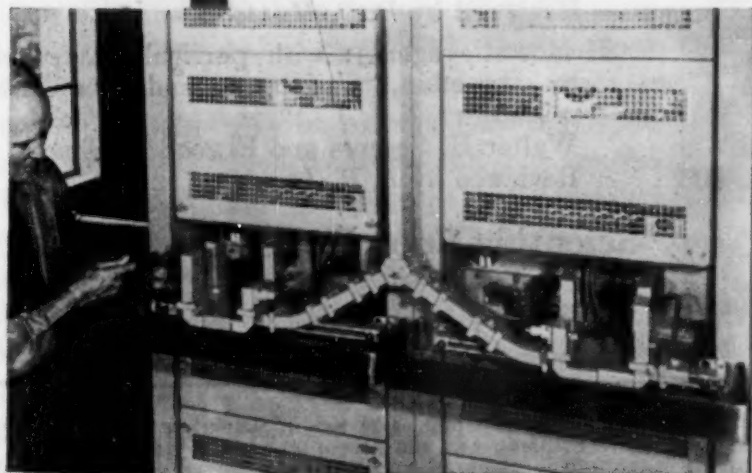
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The waveguide connects with horn antennas which are pointed toward similar antennas at the next stations miles away.



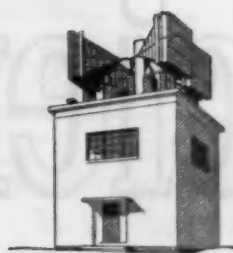
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Looking upward, the waveguide continues through the roof of the station toward the antennas.



1

Base of a waveguide circuit in a repeater station of the New York-Boston radio relay system.



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UNLIKE radio broadcast waves, microwaves are too short to be handled effectively in wire circuits. So, for carrying microwaves to and from antennas, Bell Laboratories scientists have developed circuits in "pipes," or waveguides.

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SCIENCE, November 5, 1948, Vol. 108

Oxygen Isotopes in Nature and in the Laboratory

Harold C. Urey

Institute for Nuclear Studies, University of Chicago

THAT THE ELEMENTS CONSIST OF ATOMS having different atomic weights was discovered in 1911 by Fayans and Soddy as a result of the study of radioactive elements which occur in nature. It was found that two varieties of elements could be secured having different radioactive properties but otherwise chemically identical in every respect. The theory of radioactive disintegration of uranium and thorium showed that these varieties of atoms must have different atomic weights. In particular it was found, as a result of the very careful atomic weight determinations of Theodore Richards, that samples of leads from different parts of the earth's crust had different atomic weights and, in particular, that samples of lead isolated from thorium minerals had atomic weights approaching 208, whereas those isolated from uranium minerals had atomic weights approaching 206. Sir J. J. Thompson showed that charged atoms moving through cross electrical and magnetic fields should be separated if they have different ratios of charge to mass, and hence the isotopes of the elements should be separated by such a process. He determined that this was the case for the element neon, which is nonradioactive, and hence showed that ordinary elements also consist of mixtures of atoms of different atomic weights.

It is now known that there are more than 600 varieties of atoms which make up our 96 known elements. Most of these are radioactive and have been produced by artificial means. We have found that a few elements exist only in radioactive form and thus are constantly disappearing and have been doing so since the earth's crust was created. Some have completely disappeared from the earth's crust and therefore must be made in our laboratories today. In this discussion I shall largely limit myself to one of the ordinary elements, namely, oxygen. Table 1 shows a very limited number of these varieties of atoms, those for the first 10 elements of the present periodic system. The stable isotopes are printed in heavy type and the radioactive ones in light type. These elements are very important indeed, since they contain several of the elements necessary for living processes. Also, oxygen is the most abundant element in the surface layer of the earth, namely, the layer with which we come most in contact.

This lecture was presented on the evening of September 15 in the Presidential Ballroom of the Statler Hotel, Washington, D. C., during the AAAS Centennial Celebration.

The interest in these varieties of atomic species is of several kinds. In the first place, there are the purely physical properties which physicists are studying today. During the last 25 years particularly it has been possible to unravel the laws governing the behavior of the electrons in the outer shells of the atom, and at the present time the center of the stage

TABLE 1
ISOTOPES OF THE FIRST 10 ELEMENTS

Symbol	Atomic No.	Masses
H(D)	1	1, 2, 3
He	2	3, 4, 6
Li	3	6, 7, 8
Be	4	7, 9, 10
B	5	10, 11, 12
C	6	10, 11, 12, 13, 14
N	7	13, 14, 15, 16
O	8	15, 16, 17, 18, 19
F	9	17, 18, 19, 20
Ne	10	19, 20, 21, 22, 23

of physics is held by the questions dealing with the structure of the nucleus of atoms. How are the fundamental parts held together, and what are the energy relations? The properties which are important in connection with this are the lifetimes of the radioactive nuclei, the energy of binding of the elementary particles, the nuclear spins or nuclear angular momenta, and the magnetic moments. Physicists are interested in the relative abundances of those atoms which are stable, how these varieties of atoms were produced, and what was the origin of the universe.

USES OF ISOTOPIC SPECIES

But there are many uses of these isotopic species for other sciences and such uses have been discussed many times in recent years. The use as tracers or indicators was discovered by Prof. Hevesy over 30 years ago, and the general outlines of the possible uses of such elements were made by him using naturally radioactive elements. It is, of course, natural that the many recently discovered artificial radioactive elements should be useful in this connection, especially in view of the fact that effective radioactive tracers for many of the common elements have now been discovered. There are few for which there are no satisfactory tracers of this kind, but it has been possible to separate the stable isotopes in the case of those ele-

ments for which no radioactive tracers are known, and hence tracers for these elements, hydrogen, nitrogen, oxygen, and carbon, are also available. The use of these tracers is particularly valuable in the case of the study of living processes. We have in living organisms an enormous complexity of chemical substances and chemical reactions, and every possible method that can be devised is of value if we are to understand these processes. During recent years we have heard particularly of the use of such tracers of hydrogen, carbon, nitrogen, and oxygen, since these are especially important elements in living organisms, as well as phosphorus, sulfur, iodine, sodium, potassium, and iron, which are present only in comparatively small amounts but which are nevertheless very important for the vital processes taking place.

There are other uses to which isotopes have been put besides those which we have indicated. The radioactive isotopes occurring in nature have been useful in establishing the geological time scale on a quantitative basis. Uranium and thorium decompose into lead and helium, and it is possible to measure the rate of this transformation. Uranium produces lead of an atomic weight of 206 and thorium of lead of 208. Thus, if we measure the amount of thorium and the amount of lead 208 in a mineral containing thorium, it is possible to calculate the time required for the amount of thorium present to produce the amount of lead present, and the age of the mineral could not be longer than the time so calculated. On the other hand, if we measure the amount of uranium and lead 206 in a uranium mineral, it is possible to calculate how long it would have taken for the uranium to produce the amount of lead which is present. This again would be of maximum time for the age of that mineral. Of course, if ordinary lead were present in the mineral to a small extent at the time it was deposited, an error would be made and a correction for the amount of such lead must be made. In this way a geological time scale has been established which has enabled us to date the geological periods of time with very considerable precision. The work has been done very carefully, for there are, of course, many possible errors which can be made. The analysis must be made with high precision, and the amounts of the various lead isotopes present in the samples must also be determined precisely. The oldest rocks on the surface of the earth are 1,800,000,000 years old, and ages in years of the geological periods are reasonably well known.

It is possible to calculate an upper limit for the age of the earth. The lead isotope 207 is produced from the uranium isotope 235 (the isotope of atomic bomb fame). This lead is produced more rapidly than any of the isotopes produced from thorium and

uranium. If all the lead 207 in the crust of the earth was produced from uranium 235, and none was present at the time the elements of the earth were formed, then, knowing the amount of uranium 235 and lead 207 in the crust of the earth now and the rate of transformation, we can calculate the maximum time which has elapsed since the creation of our elements as somewhat greater than 5,000,000,000 years.

Prof. A. O. Nier, of the University of Minnesota, has shown that the carbon in nature varies in isotopic composition. Living organisms, plants, and animals together with all of their probable geological remains, namely, petroleum, natural gas, and coal, contain less carbon 13 than does limestone. The origin of this fractionation of carbon isotopes is not exactly known. Differences in chemical properties of the isotope were first detected in the case of neon and the hydrogen isotopes. It was shown during the 1930s that differences in the thermodynamic properties of isotopic compounds should exist because of the differences in vibrational frequency of molecules, depending upon whether they contain one isotope or another. The early observation that the chemical properties of isotopes of elements were identical is only approximately true. Very careful measurements have shown that there are slight differences in chemical properties and that these are to be expected upon the basis of our modern knowledge of the physical properties of such molecules. It is probable that the fractionation of the carbon isotope in nature as obtained by Nier has its origin partly in such effects. It may also be that this effect is partly due to the kinetics of chemical reaction. Recently we found that algae, very simple one-celled plants, grown in Prof. Franck's laboratory, contain 2.97% less carbon 13 than the carbon dioxide in the solution in which the plants grew.¹ It may be that the chemical reaction taking place as the plant fixes the carbon of its body from the carbon dioxide in the solution favors the lighter isotope, thus producing the concentration of carbon 12 in the plant. This particular type of study has made it possible to show in other cases that deposits of carbon were due to living organisms rather than those of mineral origin and thus that life existed in the pre-Cambrian period, 600,000,000 or 700,000,000 years ago. This type of isotopic data has made a notable contribution to geological study of this kind and promises to be very fruitful in the future.

STUDIES OF OXYGEN ISOTOPIC COMPOSITION

With this rather long introduction to the subject I wish to come to the main object of this discussion,

¹ The normal ratio of C^{13} to C^{12} is 1/90, and hence this statement that the ratio for the algae carbon was .983/90 if that in the solution is 1/90.

namely, to present some recent results which my colleagues and I have secured at the University of Chicago during the last year.²

The element oxygen is the most abundant in the crust of the earth. It composes about 78% of the atmosphere, about 89% of the water, and approximately 51% of the inorganic crust of the earth. Water is the liquid in which all living processes take place. The energy which is used by all living organisms, of course, comes from the sun in the form of radiant energy. Plants are able to convert carbon dioxide and water into oxygen on the one hand and compounds of carbon on the other and thus store up chemical compounds in their tissues. These plants in turn are used by animals on the surface of the earth and burned by the aid of oxygen to produce the energy which they use in their living processes. Thus, the element oxygen, as well as carbon, is of primary importance in the living process.

The particular processes which we have been studying are those involving the deposition of oxygen in chemical compounds of the inorganic type in the earth's crust. Our study to date has been limited to calcium carbonate deposited by animals. It is to be expected that studies similar to those which I shall describe can be made on the oxygen isotopic composition in phosphates and silica, which are also deposited by animals and plants.

The ratios of the oxygen isotope in different chemical compositions as we find them in our chemical laboratories are not the same. The normal abundance of the oxygen 18 isotope is taken as very closely as 1 in 500 of the much more abundant isotope 16. But it is possible to find samples of oxygen which vary in their isotopic ratios as much as 4 or 5%; that is, from 1 part in 500 to 1.04 or 1.05 parts in 500. This is not a very large variation, though it does result in a change in the atomic weight of oxygen, as it is found in chemical substances in our laboratories, by as much as two units in the fourth decimal place. Since oxygen is the standard of atomic weight and is taken as having an atomic weight of 16, we see that this standard is not constant if we are interested in the precision of the fourth decimal place. Other elements vary in atomic weights just as oxygen does. One of the most interesting among these is chlorine, which, according to calculations which have not yet been confirmed ex-

perimentally, may vary in atomic weight by as much as 0.03 atomic weight units, i.e. by 1 part in 1,000 of the atomic weight of chlorine.

The origins of these differences in chemical properties are understood in detail in many cases. The energy and entropy and hence the free energy of chemical substances depend on the vibration frequencies of the molecules, and these depend on the masses of the atoms. Without going into the details of the mathematical calculations, we may say that the observed differences agree exactly with calculations where these are possible. If calcium carbonate is crystallized slowly in the presence of water at 0° C, the calculations show that the ratio of the oxygen isotopes in the calcium carbonate should be 1.026 to 500 if the ratio of the isotopes in the water is 1 to 500, i.e. oxygen 18 is very slightly concentrated in the calcium carbonate in relation to the water. On the other hand, if the temperature is 25° C, the oxygen isotopes will be concentrated only to the extent of 1.022 as compared with 1 in 500 in water. This shows that there is a slight temperature coefficient for the abundance of O¹⁸ isotope in the calcium carbonate as compared with that in the water. In fact, the amount of this fractionation is so slight that the atomic weight of oxygen in the calcium carbonate will be changed by only 0.0000007 atomic weight units as the temperature is changed by 1° C. A change in temperature from 0° to 25° will change the atomic weight of the oxygen by only 0.00002 atomic weight units.

Calculations of this kind were first made some 15 years ago by Dr. Greiff and myself, and during the 1930s my research group succeeded in showing that it was possible to separate the isotope of the elements by chemical methods due to small differences in the chemical properties of this kind. These methods have been used for the separation of the hydrogen, boron, carbon, nitrogen, and sulfur isotopes and are, in fact, the most effective methods for the isolation of these particular elements—the most effective in the sense that if one wishes to produce the isotopes in substantial quantities, they can be separated most cheaply by these methods. Dr. Robert White, of the University of Michigan, is engineering a chemical process for the oxygen isotopes which have previously been concentrated by distillation methods.

The temperature coefficient for the abundance of the oxygen isotope in calcium carbonate makes possible a new thermometer of great durability, which may have been buried in the rocks for hundreds of millions of years after recording the temperature of some past geological epoch and then having remained unchanged to the present time.

It is evident that, if an animal deposits calcium

² My colleagues in this case who have been partners with me in these researches over the past year are Mr. Charles McKinney, Mr. John McCrea, and Dr. Samuel Epstein, who have worked steadily on these subjects with me. Articles covering the scientific details will be published under our joint names, and this therefore is only a preliminary presentation of the scientific article which will appear in the *Bulletin of the Geological Society of America*.

carbonate in equilibrium with water in which it lives, and the shell sinks to the bottom of the sea and is buried securely in the earth and remains unchanged from that time to this, it is only necessary to determine the ratio of the isotopes of oxygen in the shell today in order to know the temperature at which the animal lived. This particular application of the chemical differences in the processes of isotopes occurred to me a year and a half ago, and since that time my colleagues and I have been trying to solve the several difficult problems encountered in making such measurements of paleotemperatures. I wish to relate some of the difficulties encountered in this problem.

IMPROVEMENT OF MASS SPECTROMETERS

The calculated differences in the ratio of oxygen 18 to oxygen 16 for 1°C difference in temperature amounts to only .0176% in that ratio. As the ratios of isotopes of this kind have not been reported in the literature with higher precision than .1%, it is immediately necessary to increase the precision of determination of these isotopic abundances by a factor of 6. In view of the excellent work which has been done on mass spectrometer in this country particularly, this is a very difficult assignment. In measurements of the ratio of isotopes the element is based upon the principle first used by Sir J. J. Thompson and Aston in England and developed particularly in this country by Prof. Dempster, of the University of Chicago, and Prof. Nier, of the University of Minnesota. Electrons are accelerated through electric fields of some 50 v and collide with gaseous molecules producing positively charged ions, which are then accelerated in a well-defined beam through high electrical fields and pass through a magnetic field. Ions having different masses but the same charge are separated from each other and can be collected on electrodes at different points. Prof. Nier has devised an instrument which collects ions of different masses on separate electrodes. The electric current produced by these ions is small, but sufficient for accurate measurement. These currents must be amplified by electronic devices in order to make measurements possible. After amplification of these small currents, the two currents are compared by means of what is essentially a Wheatstone bridge. In the work which I am describing Nier's instrument has been changed very slightly. The mass spectrometer tube (Fig. 1) has not been changed, though the electronic equipment has been quite completely redesigned. The tube which has been designed by Nier is capable of high ion beam intensity, which makes possible very precise comparisons of these ion currents. Our amplifiers are not completely satisfactory, but for limited periods of time they are sensitive and

stable. The state of balance of the bridge is recorded on a Brown potentiometer, which makes it possible for us to show the stability of the instrument over a period of time and enables us to tell whether the instrument works satisfactorily.

The second modification of the instrument which we have made consists of a rapid method of changing from one sample to another. A sample of carbon dioxide gas is confined behind a very small capillary through which it leaks into the mass spectrometer.

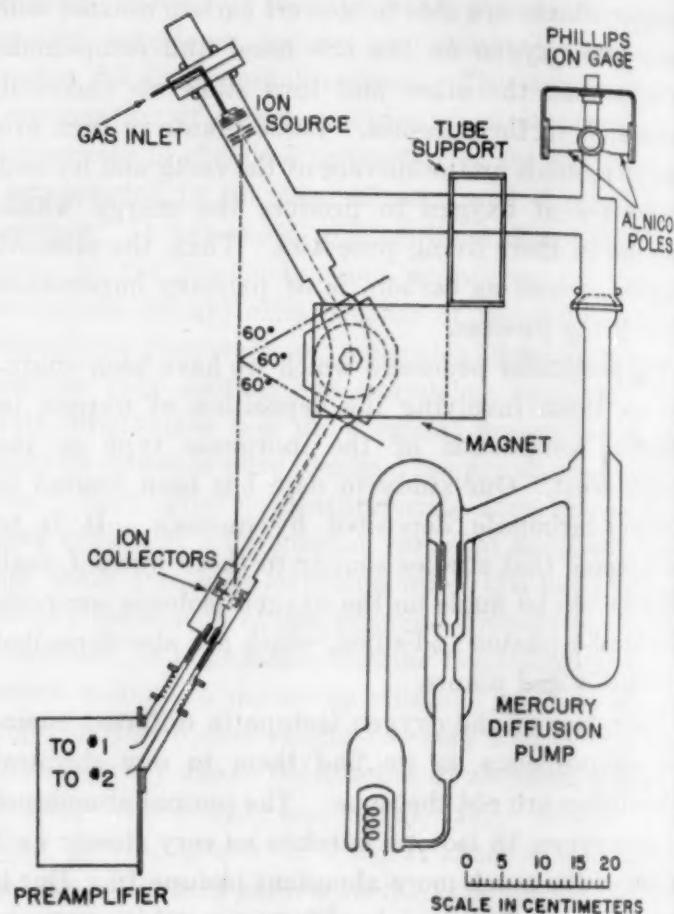


FIG. 1

We have arranged two leaks with different samples of gas behind them, with a valve which sends one sample to the mass spectrometer and the second to a waste vacuum line and then reverses the flow of the two samples. In 10 sec it is possible to shift from one sample to another. The method of operation consists in recording the state of balance on the one sample for 2 min and then switching to the other sample. The Brown potentiometer pen records the displacement from balance for first the one sample and then the other. Fig. 1 shows such a trace where the total difference is 1.2/mil of the ratio of the oxygen isotope between the two samples. This represents a difference of 4 millionths in the atomic weight of oxygen. It will be seen from the figure that it is possible to get the instrument to record small differences in isotopic abundance with very great precision.

PREPARATION OF GAS SAMPLES

If one wishes to analyze a sample of carbon dioxide with this precision, it is necessary to prepare pure samples of the gas from calcium carbonate which may be contaminated by the organic remains of the animals which secreted the calcium carbonate. In order to have a precision of 1°C it is necessary to measure the ratio of the isotopes to 0.0176%, and this means that impurities must be removed from the gas to a high degree. We use carbon dioxide as our working gas measuring masses 44 and 46. Since the 46 mass is 1/250 as abundant as 44 and we wish to secure this within 1 part in 6,000, it is necessary to remove any impurity of mass 46 to the extent of 1 part in 1,500,000. As we have found during the past 6 months, it is difficult to prepare carbon dioxide of that purity. It would be much less difficult to prepare such pure carbon dioxide if there were not the problem of preventing other oxygen from becoming mixed with the sample being investigated. The glass apparatus in which one customarily handles gases and the chemical substances which are normally used to remove impurities contain oxygen which may become mixed with the sample. In addition, the compounds of carbon and hydrogen which seem to be present in all laboratory apparatus are difficult to remove. The carbon isotopes can be handled much more easily, since laboratory apparatus does not contain this element, and impurities can be easily removed by combustion.

After trying many methods for the preparation of pure carbon dioxide we have found that a mixture of phosphoric acid and phosphorus pentoxide reacts with calcium carbonate, producing carbon dioxide of great purity and with no mixing of the oxygen of the calcium carbonate and of the phosphoric acid. All the carbon dioxide does not leave the solution immediately, but we have found that there is no fractionation of oxygen isotopes in the first sample produced as compared with the last sample. Great care must be used in placing samples in the mass spectrometer if slight fractionation of the isotopes is to be avoided. We have not been able to find impurities in a carbon dioxide prepared by this process from animal shells, from mineral calcite, and chemically prepared calcium carbonate. The most sensitive method of investigation is the mass spectrometer itself, though it is not possible to use it to test for that substance which will produce an ion of mass 46 or mass 44, the two in which we are directly interested. We are, however, able to show that the gas is pure with respect to substances which will produce ions of lower and higher mass than carbon dioxide. Finally, we have shown that samples of gas prepared in this way, when

analyzed on our sensitive mass spectrometer, give very close agreement. Table 2 shows a comparison of analyses secured by this method of preparation on the mass spectrometer which I have described. If check analyses show a difference of 0.2 per mil, the analysis

TABLE 2
DIFFERENCES IN OXYGEN ISOTOPIC RATIOS IN PARTS PER MIL BETWEEN *Haliotis rufescens* FROM MONTEREY BAY ($t = 13^{\circ}\text{C}$) AND OTHER SPECIMENS

	Sample 1	Sample 2
<i>Haliotis rufescens</i> , Monterey Bay	-0.02
<i>Pecten</i> , Bering Strait	1.32	1.08
<i>Allopora boreo-pacifica</i> , Sea of Okhotsk	0.35	0.36
<i>Pectunculus</i> , Spermonde Archipelago	-2.92	-2.92
Coral, Jamaica	-2.88	-2.90
Globigerina ooze, Pacific south of New Zealand	2.14	1.85
<i>Arca</i> , Spermonde Archipelago	-3.06	-2.90
<i>Belemnitella</i> , Upper Cretaceous, Hampshire Co., England	-1.12	-1.39
.....	-1.35
<i>Balanophyllia</i> , Monterey Bay	-2.67	-2.55
.....	-2.72

is not satisfactory; the mass spectrometer is not operating satisfactorily or some error has been made in preparing the samples. In this case the analysis is repeated.

EMPIRICAL TEMPERATURE SCALE

We turn now from the problem of a satisfactory method of analysis to the much more difficult problem of paleotemperatures. Has the ocean kept the same ratio of oxygen isotope throughout all geological time? If it has not, errors in temperature will be made. We ask what might have changed this isotope abundance. The earth began as a molten ball with oxides floating on the surface. It solidified, and rain began the erosion process. The oxygen of the water and the rocks perhaps had the same initial isotopic composition. As time went on, the igneous rocks were crumbled and carried by the rivers to other positions and were deposited as sand, clay, and limestone in other parts of the earth, and great thicknesses of these materials have accumulated. It is estimated that the oxygen in these sedimentary rocks is equal in amount to all the oxygen in the ocean and perhaps is three times as great. If the concentration of O^{18} in the igneous rocks is not the same as in sedimentary rocks, the difference must have been supplied from the ocean, and its isotopic composition must be changed. I think it probable that the oxygen of sandstone and much of that of shale has not been changed much in this weathering process. It is a subject which we shall investigate, but for the purpose of my present discussion the total time from the Cretaceous to the present is only 60,000,000 years, or only a small fraction of the total time that erosion has

taken place. Simple calculations show that not much change in isotopic composition could have occurred in that time.

We are investigating the shells of living organisms which have a capacity to fractionate chemical elements to a high degree. Some plants, for example, concentrate iodine from the sea water in concentrations that are very much greater than exist in the sea. Some animals concentrate copper or vanadium from very low concentrations of these elements in sea water. It is always possible that an animal will fractionate the oxygen isotopes, and we fully expect to find some cases of this kind. But it does seem probable that such effects will be rare in the case of inorganic deposits such as calcium carbonate.

Let us assume that an animal does lay down its calcium carbonate in equilibrium with the sea and now enquire into what happens as the animal is buried and becomes converted to a fossil. It is possible, and I think probable in some cases at least, that the oxygen of the shell will exchange places with the water surrounding the shell. This should not be a very fast process, since it depends on the rate of diffusion of the oxygen through the solid matter. Estimates as to the velocity of this process have led me to the conclusion that the process will take place in the finest material in a matter of years to thousands of years, but in the case of coarse crystals it will not occur within a time of the order of 1,000,000 to 1,000,000,000 years. In any case we wish to secure heavy, thick, massive crystals of calcium carbonate for our study in order to increase our probabilities of success. We have found cases in which these diffusion effects have occurred but also, we believe, cases in which they have not.

In order to get a temperature scale it is necessary to establish empirically a relationship between the isotopic composition of the shells of the present-day animals and the temperatures at which they live, since the theory is only approximately applicable. To do this, it is necessary to use animals which have lived in sea water of full salinity in order to avoid the possibility that fresh water, which may have an isotopic composition different from that of sea water, has changed the isotopic ratio of the oxygen of the water in which the animal lived so that the isotopic ratio would not be characteristic of the temperature alone. It proves difficult to discover such places on the earth's surface at the present time, since most of the shallow seas of the world are brackish to a large degree. It is also difficult to be sure of the temperatures of the water in which the animal lived, since temperature of the sea fluctuates and most animals wander from one temperature zone to another. Many people have helped us to secure specimens of animals. Dr. L. F. de

Beaufort and Dr. de Jong, of Amsterdam, have secured samples from the Dutch East Indies; The Chicago Museum of Natural History, from Hawaii; Dr. H. S. Brown, from Jamaica; Dr. L. R. Blinks, of the Hopkins Marine Station, from Monterey Bay; and Dr. Robert S. Dietz, from Bering Strait and from the bottom of the Pacific Ocean south of New Zealand and Australia. We also received a sample from Dr. Blinks from the Sea of Okhotsk. Dr. Austin H. Clark, of the Smithsonian Institution, supplied us with some samples of his crinoids taken from various parts of the world. We have not as yet investigated all the samples of this kind which we have received. Fig. 2 shows the plot of the recorded temperature against the isotopic composition for a number of specimens.

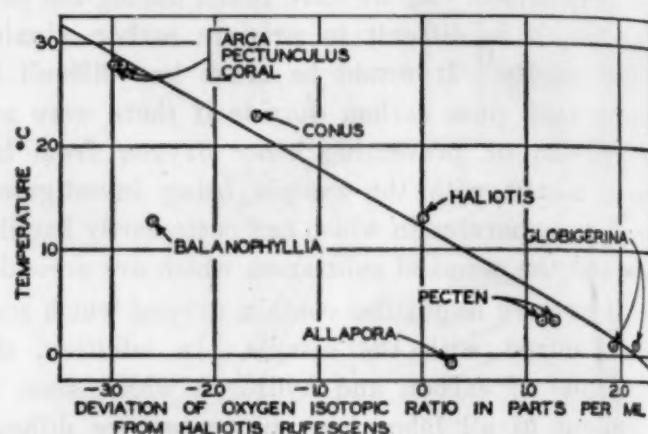


FIG. 2. The specimens included are from Spermonde Archipelago, Dutch East Indies (*Arca* and *Pectunculus*); Hawaii (*Conus striatus*); Monterey Bay, California (*Haliotis rufescens* and *Balanophyllia elegans*); the bottom of the Pacific, latitude 60° 13' S, longitude 147° 45' E (*Globigerina* ooze); Bering Strait (*Pecten*); and the Sea of Okhotsk (*Allapora boreo-pacifica*).

The latter is given in parts per thousand of the ratio of O^{18} to O^{16} compared to an abalone (*Haliotis rufescens*) from Monterey Bay, the temperature of which is taken as 13° C. It will be noted that a number of the points on this curve follow rather well on a straight line, the slope of which is very close to the calculated slope, 4.4 per mil between 0° C and 25° C. The Bering Strait samples do not fall well on the curve, but the Bering Sea is slightly brackish and reasonable estimates in regard to the isotopic deviation expected would move this point toward the curve. The specimen from Hawaii falls above the curve, indicating that this animal (a gastropod, *Conus striatus*) lived perhaps at a lower temperature than is assumed. The points for the coral from Monterey Bay do not fall anywhere near the curve, and at present no certain explanation of this difficulty is possible. It may be that such finely divided materials as corals exchange their oxygen with water of the air in a reasonable length of time. In general, every compact shell which we have investigated lies on the curve, and every point off the curve is that of an organism having a

loose structure and collected some 50 years ago. All of the crinoids investigated to date belong to this group, and it is well known that they have an extremely porous structure in their skeleton. Our conclusion from this curve is that many organisms do fit the theoretical curve expected on the assumption that the calcium carbonate deposited is in equilibrium with the sea water.

The fact that we have such great difficulty in finding suitable specimens for investigation today means that similar difficulties would have been encountered in past geological periods. However, since the land surface of the earth is exceptionally large at the present time, we may expect that brackish water will be a far more common occurrence on the surface of the earth today than in the past. In general, we must attempt to select our specimens from those deposits which from all geological evidence indicate fully marine conditions. A study of the various types of animals which might fit these conditions early led us to consider two types as particularly worthy of study. The first was the crinoids, which belong to the echinoderms, which are entirely marine in their habits though some specimens do live in quite brackish water but never in fresh water. Since the skeletons of the crinoids are very porous, consisting of a three-dimensional, lace-like structure, these appear to be unsatisfactory on these grounds. The second group of animals which we consider are the cephalopods, which are entirely marine animals and among which the belemnites seem to be particularly suitable. The belemnites, which lived during the Mesozoic era, are cephalopods similar in general structure to the modern squid. They had an internal skeleton of calcite. A typical specimen would be perhaps as large as a cigar and of somewhat the same shape, with a rather wide flaring cone in one end. Its transverse section shows that it consists of crystals of calcite arranged radially from the center of the specimen. This is a characteristic arrangement of the crystals and a well-preserved specimen is always translucent, sometimes nearly the color of honey and grading to darker shades of yellow and brown. It would appear that this deposit of calcite is the original deposit (with about as high degree of certainty as can be expected in matters of this kind). We have, then, a marine type of animal with a heavy, substantial skeleton well suited for the preservation of the original isotopic composition of the shell.

TEMPERATURE OF THE UPPER CRETACEOUS OF HAMPSHIRE COUNTY, ENGLAND

Dr. Stubblefield, of the London Geological Museum, to whom we are much indebted, supplied us with a number of specimens of belemnites, oysters, and

brachiopods from the upper Cretaceous of England, nicely classified, arranged in the order in which they were deposited in geological time. In fact, it has only been necessary for us to determine the isotopic ratios and fit them into the outline of the research supplied by him. Our work to date has completed the study of the belemnites, and work is continuing on the oysters and brachiopods as well as the chalk in which they were embedded. The temperatures so secured (Table 3) range from 17° or 18° C to 27° C. There is a trend in these results, but this trend cannot be taken seriously on so few specimens. One could hardly judge the climatic condition in any sea of the

TABLE 3
TEMPERATURES OF BELEMNITES FROM THE UPPER CRETACEOUS OF HAMPSHIRE COUNTY, ENGLAND

Zone	Specimen	Analysis	Avg.	Temp.	Chalk analysis
Upper Chalk	<i>Belemnitella</i>	-1.26			
	<i>Ostrea lunata mucronata</i>	-1.08	-1.14	18.8	-2.64
		-1.07			
Upper Chalk	<i>B. mucronata</i>	-1.39			
	<i>B. mucronata</i>	-1.35	-1.29	19.7	-3.38
		-1.12			
Upper Chalk	<i>Actinocamax</i>	-1.71			
	<i>Actinocamax quadratus</i>	-1.76	-1.73	22.1
Upper Chalk	<i>Actinocamax</i>	-2.18			
	<i>Offaster pilula</i> sp.	-2.25	-2.21	24.7
Upper Chalk	<i>Actinocamax</i>	-2.57			
	<i>Marsupites testudinarius</i> sp.	-2.52	-2.54	26.5
Lower Chalk	<i>A. plenus</i>	-0.91			
	<i>Holaster subglobosus</i>	-0.92	-0.91	17.5

earth at the present time by the investigation of a single or even a few specimens of the animals that live there now, and since we have only some half-dozen specimens to record the climatic conditions of approximately 10,000,000 years, it will be easily seen that no very serious conclusions can be drawn. The results of our measurements, however, are in accord with the views of the geologists deduced from the kinds and types of animals living in the Cretaceous as to the probable temperature of that part of the earth during this period.

The data thus far secured are not sufficient to draw extensive and varied conclusions in regard to past geological temperatures, but they are sufficient to lead us to believe that at least some measurements of past temperatures can be made, and hence a quantitative basis for past climatic conditions of the earth secured. We cannot expect that every fossil which has been or will be found on the surface

of the earth can be tested by our methods for the temperature at which it lived. We do hope, however, to find a small fraction of such fossil remains preserved to such a degree that such measurements can be made and at least a limited exact knowledge in regard to these matters secured. These studies can be compared to the radioactive time scale which I referred to previously. That method is very simple

in principle, but the actual carrying out of the search which established the time scale involved very careful work covering many years. What will be remarkable, if these ideas are substantiated by further work, will be that such a transient physical quantity as temperature will prove to have been recorded in the rocks in a sufficiently durable form to allow us to read this thermometer at the present time.

NEWS and Notes

Albert E. Whitford has been appointed director of the Washburn Observatory, University of Wisconsin, succeeding Joel Stebbins, who retired on July 1.

Z. I. Kertesz, professor of chemistry at the New York State Agricultural Experiment Station, Cornell University, Geneva, has been granted a sabbatical leave and has accepted a joint invitation from the Division of Food Preservation and Transport, CSIR, the Australian Chemical Institute, and the Food Technology Association to study for 6 months the biochemical aspects of food production and processing in Australia. Dr. Kertesz leaves Geneva early this month. His headquarters will be at the Chemistry Department, Sydney Technical College, Ultimo, Sydney, N.S.W.

Stanley D. Miroyiannis has resigned as professor and chairman of the Department of Biology at Northeastern University, Boston, to accept the position of professor of advanced biology in the Graduate School of the Massachusetts College of Pharmacy, Boston.

Robert Simha, consultant for the Division of Organic and Fibrous Materials, National Bureau of Standards, is spending four months in Europe studying the status and trends of high-polymer research in government, academic, and industrial institutions. In September he attended the International Rheological Congress in Holland; in October he lectured at the Institute of Physical Chemistry, Basel,

Switzerland; and he is now lecturing at the University of Stockholm.

Theodore L. Jahn, who has been associate professor of zoology at the State University of Iowa, is now professor of zoology on the Los Angeles campus of the University of California. In addition to teaching general physiology and physiology of the Protozoa, Dr. Jahn will continue his research on the physiology of vision.

Robert W. Dougherty, who was formerly associated with the College of Veterinary Medicine, State College of Washington, has recently been appointed professor of veterinary physiology at the New York State Veterinary College, Cornell University.

Adam G. Bøving, research associate in zoology, Smithsonian Institution, has been elected a member of the Royal Academy of Sciences and Letters of Denmark.

Elmer L. Sevringhaus, director of endocrine and metabolic clinical studies at the Medical Center, Jersey City, and director of clinical research for Hoffman-La Roche at Nutley, New Jersey, has also been appointed clinical professor in the Department of Medicine of the New York Medical College, with teaching and clinical duties at the Metropolitan Hospital in connection with endocrine and nutritional work.

C. H. Hardin Branch, formerly executive director of the Institute of Pennsylvania Hospital at Philadelphia, has been appointed professor and head of the newly formed Department of Psychiatry at the University of Utah College of Medicine.

Keith T. Swartz, formerly with the Research Department of the Continental Can Company, Chicago, has recently joined the staff of the Animal

Products Branch, Quartermaster Food and Container Institute for the Armed Forces, Chicago. Dr. Swartz will be engaged in developmental work on canned meat items for use by the Armed Forces.

Harold A. Zahl, who has been associated with the Signal Corps in research and development work since 1931, has just been made director of research for the SC Engineering Laboratories, Fort Monmouth, New Jersey.

Horace W. Stunkard, professor and head of the Department of Biology, New York University, recently returned from sabbatical leave at the Scripps Institution of Oceanography, La Jolla, California. During his leave, W. W. Cort, of Johns Hopkins University, served as chairman of the Editorial Committee and managing editor of the *Journal of Parasitology*. Volume 34 (1948) is now complete and manuscripts intended for publication in the journal should henceforth be sent to New York University, University Heights, New York City 53.

Visitors to U. S.

Torbjoern O. Caspersson, director of medical cell research and genetics at the Medical Nobel Institute, Karolinska Institute, Stockholm, is to present the Salmon Memorial Lecture this fall. Dr. Caspersson's lecture on "Cell Function and Cell Growth in Normal and Pathological Conditions Studied by Quantitative Cytochemical Procedures," will be given November 8, 9, and 10, at 8:30 P.M. in Hoesly Hall of the New York Academy of Medicine, 2 East 103rd Street, New York City.

Two German agricultural scientists, William Rudolf, director of the Kaiser Wilhelm Research Institute at Voldagsen, and Alfred Koenekamp,

Director of the Grassland Fodder Crop Institute at Voelkenrode, have just completed a four-day visit at Iowa State College. The two men, sent to this country under the auspices of the U. S. occupation authorities in Germany, are making a tour of some of the chief agricultural colleges.

Grants and Awards

Charles P. Berkey, Newberry professor emeritus of geology at Columbia University, has been named first recipient of the Kemp Medal by the trustees of Columbia upon recommendation of the advisory council of the Kemp Memorial Fund "for distinguished service in geology." This award was established last year in honor of James Furman Kemp, founder of the Geology Department. The presentation was made by President Eisenhower at the Men's Faculty Club on Tuesday, October 26. Dr. Berkey was recognized for his early pioneering work in engineering geology and also for his aid and advice on some of the major engineering projects of this century, including the George Washington Bridge, the Lincoln Tunnel, the Grand Coulee, the TVA, and other great dam sites.

David S. Grey, a member of the research staff of the Polaroid Corporation, Cambridge, Massachusetts, received the 1948 Adolph Lomb Medal on October 22 during the 33rd annual meeting of the Optical Society of America. The award is given every two years to "a young scientist of outstanding promise who has made a noteworthy contribution to optics." Mr. Grey's accomplishments have included the design of lenses for television-receiving sets and microscopes for medical research, as well as the development of an ultra-high-speed lens for use with radar. One of his most recent developments promises to bring about sharper and brighter images in television sets of the projection type.

Vannevar Bush, president of the Carnegie Institution of Washington and until recently chairman of the Research and Development Board of the National Military Establishment, has received the 1949 medal of the Industrial Research Institute, Inc.

The award, established in 1945, is given for outstanding accomplishment in the management field of industrial research. Dr. Bush received the award for his leadership in the OSRD, in marshaling industrial and academic research and coordinating it with the military effort for the common defense.

Applications for grants in aid of research on cardiovascular problems to begin in 1949 will be received by the Life Insurance Medical Research Fund up to January 15, 1949. Support is available for physiological, biochemical, and pathological research which bears on cardiovascular problems, as well as for clinical investigation in this field. Preference is given to fundamental research. It is expected that about \$500,000 will be awarded for these grants.

Applications for postgraduate fellowships for training in research in 1949-50 will be received by this Fund up to January 1, 1949. Preference is given to candidates who wish to work in the broad field of cardiovascular function or disease and to candidates who wish to work in institutions other than those in which they have obtained most of their experience. A doctor's degree (M.D. or Ph.D.) or the equivalent is required. The annual stipend usually varies between \$2,500 and \$3,500, but larger amounts are granted in special cases. Approximately 12 fellowships will be available.

Later in the year, the Fund will also offer a number of student (predoctoral) research fellowships for 1949-50.

Both grants and fellowships will become available on July 1, 1949. Further information and application blanks may be secured from the Scientific Director, Life Insurance Medical Research Fund, 2 East 103rd Street, New York 29, New York.

Fellowships

The first Psychometric Fellowships, established this year by the Educational Testing Service for graduate study under the new Psychometric Training Program in the Department of Psychology at Princeton University, have been awarded to Bert F. Green, Jr., a student at Yale University, and Warren S. Torgerson, who has recently completed a year's graduate study at

the University of Wisconsin. The fellowships are normally renewable and carry a stipend of \$2,200 annually. Holders may engage in part-time research at the Educational Testing Service as well as full-time study toward the doctorate. The new program, inaugurated in September, is being directed by Harold Gulliksen, research adviser to the ETS and professor of psychology at the University. In addition to the faculties of the Departments of Psychology and Mathematics, the staff of the ETS, which is a nonprofit testing agency, is assisting in the program.

The American Heart Association announces that applications for fellowships and for research in cardiovascular disease are available. Application blanks may be obtained by addressing the Medical Director, American Heart Association, 1775 Broadway, New York 19, New York.

The ultimate aim of the Association is to develop a continuing program of productive research within the broad field of cardiovascular disease, including rheumatic heart disease.

The recommendations of the Research Policy Committee were published in the *American Heart Journal*, 1948, 36, 463. These policies are subject to modification by the membership of the Association's Scientific Council and approval by the Board of Directors.

The research program of the American Heart Association will be closely coordinated with that of the National Heart Institute of the National Institutes of Health, U. S. Public Health Service, and with that of the Life Insurance Medical Research Fund.

Colleges and Universities

Ohio State University's Chemistry Department is planning a program November 19-20 to commemorate the University's 75th anniversary. Graduates of the Department will read papers and a dinner will be held November 19. Those holding advanced degrees in chemistry from Ohio State have been invited to the meeting. Faculty members who are arranging the program are Frank Verhoek, chairman, Cecil E. Boord, and William MacNevin.

A new electrical engineering building is to be started at Iowa State College within the next few weeks, according to Charles E. Friley, president of the College. Allotment of \$858,000 for the building has been approved by the interim committee of the state legislature.

Lehigh University has received a graduate research fellowship, valued at \$2,000, from the Socony-Vacuum Company for research in the general field of instrumental analysis. The fellowship was assigned to the Department of Chemistry, and Earl J. Serfass, chemistry professor, will direct the work. The Lehigh fellowship, which is one of 13 sponsored by Socony-Vacuum over the country, is the only one for the support of research in analytical chemistry.

The Department of Milling Industry, Kansas State College, has just completed, at a cost of \$20,000, a new pilot plant bakery. The bakery, funds for which were contributed by the milling industry, was designed for research on wheat quality and fermentation problems and is fully equipped for a wide variety of research activities. According to J. A. Shellenberger, head of the Department, who has just returned from a two-month assignment in Costa Rica and El Salvador for the Food Supply Division of the Institute of Inter-American Affairs, this is the only laboratory of its kind connected with an educational institution or an agricultural experiment station in the United States. The equipment will be used to a limited extent in connection with the laboratory portion of a course which is offered in experimental baking.

Additions to the faculty of California Institute of Technology during the last 15 months have brought the staff to a total of 318 as compared with 264 a year ago. The ratio of teachers to students is now one of the lowest in the country (approximately one teacher for every four students). In addition to 4 associate professors, 2 assistant professors, 22 research associates and 6 instructors, 55 research fellows were appointed, 25 of whom are from foreign countries.

The highest laboratory in the world, situated on the summit of Mt.

Evans, Colorado, at an elevation of 14,156 feet, is currently being used by a number of universities for cosmic-ray research and for biological experiments. Established in 1936 through the generosity of John Evans, after whose grandfather the mountain was named, the laboratory has since the war been administered by an inter-university group composed of New York University, Chicago, Cornell, M. I. T., Denver, and Princeton. During the war the laboratory was used as a Meteorology Station by the Army. Because of the steadily increasing interest in cosmic-ray research, space in the laboratory itself has become insufficient. Shown in the cover photo, taken by S. A. Korff, of New York University, are a large trailer housing the University of Denver biological experiment, a station wagon which transports the New York University cosmic-ray equipment, and mobile equipment from the University of Chicago and M. I. T. The small stone building on the far right houses the electric power-generating units.

Industrial Laboratories

J. A. Hutcheson, director of the Westinghouse Research Laboratories, has received the Westinghouse Order of Merit for outstanding engineering achievements and able direction of research activities. Highest award of the Westinghouse Electric Corporation to its employees, the Order of Merit is conferred by vote of the Company's Board of Directors. Dr. Hutcheson was cited for "his valuable engineering contributions to the development of radio broadcasting equipment, military radar, and other electronic apparatus," and for "his capable management and direction of the Research Laboratories."

Donald K. Morgan, formerly research engineer of the Hartford-Empire Company, has been appointed chief engineer of John I. Thompson & Company, Washington, D. C. He succeeds Charles J. Roggi, who resigned on October 1.

S. C. Ogburn, Jr., head of the Department of Chemical Engineering at Bucknell University from 1928 to 1936 and more recently research and development manager for the Pennsylvania Salt Manufacturing Company,

Philadelphia, has been appointed manager of research and development and chairman of the Research and Development Committee for the Foots Mineral Company of Philadelphia.

Meetings and Elections

The Engineering College Research Council will meet November 8 in Washington, D. C. The Research Council, representing the research activities of 73 institutional members of the American Society for Engineering Education, will bring together at this meeting engineering research administrators, news writers, and editors. The papers to be given are: "Applied Science in the Daily Press," by Herbert B. Nichols, science editor of the *Christian Science Monitor*; "The 'Working Press,'" by John M. McCullough, of the editorial staff of the *Philadelphia Inquirer*; "Science Service," by Ron Ross, news editor of that organization; "Photographs and Diagrams: How the Magazines Can Help," by Edward D. Fales, associate editor of *Science Illustrated*; "Science on the Radio," by Irving J. Gitlin, CBS science director; "The Business Press," by Paul Wooton, president of the National Conference of Business Paper Editors; and "Research in the Engineering Press," by Philip W. Swain, editor of *Power*.

The Polytechnic Institute of Brooklyn and the Brooklyn Polytechnic Chapter of the Society of Sigma Xi will hold a symposium on "The Solid State" on Saturday, November 13, at 10 A.M., in the Student Lounge of the Institute, 99 Livingston Street, Brooklyn. Max von Laue, of the University of Göttingen, will make the introductory remarks and will be followed by C. G. Shull, Oak Ridge National Laboratory, who will speak on "Techniques and Applications of Neutron Diffraction"; Rudolph Brill, Phillips Petroleum Company, whose topic will be "Some X-Ray Studies of Chemical Bonding"; and Sir W. L. Bragg, University of Cambridge, who will discuss "A Dynamical Model of a Crystal Structure."

The National Malaria Society will meet conjointly with the American Society of Tropical Medicine, the American Academy of Tropical Medi-

ine, and the American Society of Parasitologists in New Orleans, December 5-8.

The National Malaria Society has scheduled four scientific sessions, including a panel discussion on malaria and a joint meeting with the American Society of Parasitologists and the American Society of Tropical Medicine. Panel discussions will also be held by the American Society of Parasitologists on arthropod vectors and the American Society of Tropical Medicine on helminths and protozoa.

Registration will begin Sunday afternoon, December 5, at the Hotel Roosevelt, which will be the headquarters.

More detailed information about the meetings may be obtained from the secretaries of the societies concerned: Martin D. Young, P. O. Box 1344, Columbia, South Carolina (Malaria); Harold W. Brown, 600 West 168th Street, New York City 32 (Parasitology); Frederick J. Brady, National Institutes of Health, Bethesda, Maryland (Society of Tropical Medicine); and E. C. Faust, Tulane University, New Orleans, Louisiana (Academy of Tropical Medicine).

The Second Inter-American Congress on Brucellosis will be held November 17-20 at Mendoza, and November 22-26 at Buenos Aires, Argentina, under the auspices of the Argentine Government and the Pan American Sanitary Bureau. Some of the topics to be discussed are: the investigations of brucellosis within the different countries including Colombia, Venezuela, Chile, United States, Puerto Rico, and Mexico; human brucellosis; zoological and neurological manifestations of brucellosis; and treatment of brucellosis with streptomycin and sulfadiazine. On November 19 and 20 there will be excursions to the laboratories, hospitals, dairy establishments, meat-packing plants, farms, etc. The meeting then moves to Buenos Aires, and excursions in that city will be made on November 24.

The U. S. National Commission for UNESCO met in Boston September 27-29 for the purpose of analyzing UNESCO's proposed program for 1949. Nine of the 10 scientists on the Commission attended the meetings. The program for the Natural Sciences

was examined in detail at two Section meetings, with the scientists and engineers of the Commission and half a dozen specially invited guests participating in the discussions.

The Section meeting of the Natural Sciences assigned the highest priority to the development and further strengthening of UNESCO's four Field Science Cooperation Offices and to UNESCO's program of "Grants-in-Aid" to the International Scientific Unions. The Section further commended UNESCO for its work in the field of scientific reconstruction and urged the development of a "Science Credits Scheme" and of activities directed toward easing import and export regulations and toward exemption from currency controls in reconstruction work. The Section approved the maintenance by UNESCO in Paris of a World Center of Scientific Liaison, including among its activities, in addition to those mentioned above, improvements of scientific documentation, the international exchange of scientists, the maintenance of a Scientific Apparatus Information Section, and close collaboration with the United Nations and the specialized agencies. The scientists meeting at the Section of the Natural Sciences in Boston gave lowest priority to the following two projects in the 1949 program: (1) the standardization of scientific terminology and the preparation of dictionaries; (2) activities in the field of cartographic science.

The Section meeting of the Natural Sciences, as well as the entire National Commission, went on record as favoring full participation by UNESCO in the forthcoming United Nations Scientific Conference on the Conservation and Utilization of Natural Resources (May-June 1949; see Bulletin 8, "Science in UNESCO," issued by the NRC Committee on UNESCO). The Section meeting expressed its approval of the appointment by the U. S. National Commission of a Panel on the Protection of Nature, with Harold J. Coolidge as chairman. It also recommended that "in its participation with the United Nations Natural Resources Program, UNESCO should put special emphasis on the preservation of natural areas which have particular importance for

their aesthetic and nonmaterialistic values."

The Section meeting expressed much interest in UNESCO's work in the field of the popularization of science and welcomed the formation of a panel on the subject under the guidance of Mr. Watson Davis. It was recommended that the science clubs of the United States should cooperate with students abroad in science projects.

There was much discussion about barriers to the free movement of scientists, and the Section meeting urged that the need for simplification of visa requirements be promptly brought to the attention of the Department of State and of the Immigration and Naturalization Services of the Department of Justice.

At the Section meeting the United Nations-UNESCO inquiry into the establishment of international laboratories and observatories was discussed, and, specifically, it was recommended that an interorganization committee be set up for the detailed study of a project to establish somewhere in Europe an international computational center and associated international astronomical laboratory.

A considerable amount of time was devoted to a discussion of two questions relating to science and the maintenance of peace. The Section meeting was presented with an interim report on the subject by the NRC Committee on UNESCO. The most significant contribution to the discussion was made by Arthur H. Compton, whose remarks led to the adoption of the following resolution incorporated in the report of the Section meeting:

"We propose the following four ways in which UNESCO can use science toward the maintenance of peace:

"(1) Scientists can emphasize and develop the human values associated with science and technology.

"(2) Scientists can insist on freedom and honesty in their search for knowledge.

"(3) Because of the natural oneworldness of their fields, scientists can consciously serve as prototypes of world citizens.

"(4) By systematically promoting international cooperation, scientists can contribute directly to world inte-

gration and the construction of the defenses of peace."

A limited amount of mimeographed material relating to UNESCO's activities in the field of the natural sciences is obtainable upon request from the NRC Committee on UNESCO, 2101 Constitution Avenue, Washington 25, D. C.—BART J. BOK, *Harvard College Observatory*.

The American Society of Limnology and Oceanography (formerly the Limnological Society of America) held its 11th annual meeting at the University of Maryland, College Park, on September 10-12. This was the Society's first meeting since its expansion to include the marine field (*Science*, March 26, p. 318). The sessions were attended by more than 100 members and included, in addition to the usual volunteer papers, a demonstration session, invitation symposia, and a field excursion. The symposium on the "Ecology of Inshore Waters" was held jointly with the Ecological Society of America, and that on "The Optimum Catch" was sponsored jointly with the Ecological Society and the Eastern North American Region of the Biometric Society. The field excursion to the Chesapeake Biological Laboratory included a demonstration by boat of methods for oyster and crab investigations.

At the business meeting of the Society, C. E. ZoBell, Scripps Institution of Oceanography, University of California, was elected president, and D. C. Chandler, Franz Theodore Stone Laboratory, Ohio State University, vice-president. G. L. Clarke, Biological Laboratories, Harvard University, continues as secretary-treasurer. The Society voted to establish a Pacific Division which will include all members west of the Rockies and will hold its own regional meetings. The Oceanographic Society of the Pacific was invited to join in this step, and on October 6, 1948, this organization voted to disband as such and to amalgamate with the American Society of Limnology and Oceanography in forming the new Pacific Division. All members of the former Oceanographic Society of the Pacific thus automatically have become members of the American Society of Limnology and Oceanography and are included in

the Pacific Division. C. L. Hubbs, Scripps Institution of Oceanography, was appointed vice-president, and R. P. Dempster, California Academy of Sciences, was appointed secretary of the Pacific Division to serve until the first meeting. With the establishment of the Pacific Division, the American Society of Limnology and Oceanography now has a total enrollment of about 700 members.—GEORGE L. CLARKE, *Secretary-Treasurer*.

The Engineering Foundation has elected Joel D. Justin, consulting engineer of Philadelphia, as its chairman, according to John H. R. Arms, secretary of the Foundation. Boris A. Bakhmeteff, consulting engineer and professor of civil engineering, Columbia, was chosen vice-chairman. Re-elected officers were Edwin H. Colpitts as director, and Mr. Arms, secretary. In addition to Mr. Justin and Mr. Arms the Executive Committee will consist of: O. H. Buckley, president of the Bell Telephone Laboratories; A. B. Kinzel, vice-president, Union Carbide and Carbon Research Laboratories; R. H. Chambers, former vice-president and consulting engineer of the Foundation Company; and Herman Weisberg, mechanical engineer in the Electrical Engineering Department, Public Service Company, New Jersey.

The Research Procedure Committee will be headed by Dr. Bakhmeteff. During the past year the Engineering Foundation has aided 18 research projects, which included studies in such varied fields as hydraulics, alloys of iron, properties of gases and gas mixtures, riveted and bolted structural joints, welding, and properties of metals at different temperatures. The Foundation will continue 9 of the 18 projects and add 5 more to the list this year.

Deaths

George A. Dick, 70, professor emeritus of animal husbandry and former dean of the University of Pennsylvania's School of Veterinary Medicine, died October 15 at University Hospital, Philadelphia.

C. Walter Collins, 66, who, prior to his retirement in 1944, was senior entomologist in charge of the U. S. Department of Agriculture's Forest

Insect Laboratory in Morristown, New Jersey, died October 18 at his home in Morristown.

Daniel E. Ziskin, 53, professor of dentistry at Columbia's School of Dental and Oral Surgery and head of the Division of Oral Diagnosis, died October 21 in New York City.

"The Future in Medicine" will be the general theme of the 14th series of Laity Lectures to be given by the New York Academy of Medicine this year. Admission to these lectures at 2 East 103rd Street, New York City, is free, and the public is cordially invited to attend. The lectures, all of which will be at 8:30 P.M., will also be broadcast over WNYC and WNYC-FM. Speakers and their subjects follow: November 17, Robert Patterson, former Secretary of War, "Some Problems in Law and Medicine"; December 9, Ephraim Shorr, Cornell University Medical College, "The Endocrines: Masters or Servants?"; December 23, Leo Alexander, Boston State Hospital, "Science Under Dictatorship"; January 13, William C. Boyd, Boston University School of Medicine, "Blood and Man"; January 27, John R. Dunning, Columbia University, "The Future of Nuclear Energy"; and February 10, George E. Gardner, Judge Baker Guidance Center, Boston, "The Criminal in Our Midst."

Make Plans for—

American Mathematical Society, November 27, Los Angeles, California.

Conference on Electronic Instrumentation in Nucleonics and Medicine, sponsored by the Institute of Radio Engineers and American Institute of Electrical Engineers, November 29-December 1, New York City.

American Medical Association, interim session, November 30-December 3, St. Louis, Missouri.

American Academy of Dental Medicine, annual midwinter meeting, December 5, Hotel Pennsylvania, New York City.

Highway Research Board, 28th annual meeting, December 7-10, National Academy of Sciences, Washington, D. C.

TECHNICAL PAPERS

The Amino Acid Content of Bacteriophage

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Methods of partition chromatography (1) require such small quantities of material that they provide a way to investigate the amino acid content of purified viruses which are available only in minute amounts. One of the most convenient virus systems to be studied in this way consists of bacteriophages and their host organisms.

TABLE 1
AMINO ACID CONTENTS OF *E. coli* AND T (4) BACTERIOPHAGE

Amino acid	Percentage*	
	In <i>E. coli</i>	In T(4)
Aspartic acid	9.57	11.97
Glutamic acid	9.59	11.97
Serine	4.88	4.77
Glycine	7.94	7.34
Threonine	5.31	7.00
Alanine	8.40	9.40
Valine	5.00	6.51
Methionine	2.92	< 1.3
Phenyl alanine	4.80	4.16
Isoleucine	4.63	3.90
Leucine	8.68	6.51
Tryptophane	1.29
Proline	3.02	5.00
Tyrosine	4.33	3.74
Arginine	8.21	6.51
Lysine	8.26	8.46
Histidine	3.26	< 2.6

* Expressed as percentage of total amino acids found on paper.

With this in mind, we have been analyzing *E. coli* and several of its bacteriophages. Results of chromatographic analysis of the organisms are being published elsewhere (2). Preliminary results of a corresponding analysis of the T(4) strain of its bacteriophage are reported here.

The quantitative methods of filter paper chromatography employed (2, 3) have been the same as those described in connection with the analysis of *E. coli*. The preparation of bacteriophage was one that had been purified by ultracentrifugation. It was hydrolyzed in the same way as the bacteria and otherwise handled in the same fashion; the amino acid content determined for it is listed in Table 1, along with the results on *E. coli* calculated in terms of the per cents of each amino acid

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referred to the total amount of amino acid found on the chromatogram. Evidently the same amino acids are present in both the bacterial and the bacteriophage suspensions. There are some differences in the relative amounts of these amino acids in the two preparations, but, for the reasons stated below, these differences cannot yet be considered as significant.

The greatest uncertainty in this work lies not in the results of the analytical procedures but rather in the difficulties in getting sufficiently pure bacteriophage suspensions. Electron micrographic observation indicated that the suspension of bacteriophage consisted predominantly of the well-known sperm-like particles of this virus; but, though this demonstrates that the preparation had been largely purified by the ultracentrifugation to which it had been subjected, it is not an adequate proof of chemical purity. The final proof of purity must be consistency of analytical results with repeated purification. Considerable progress is still being made in the development of methods that can yield relatively large amounts of increasingly pure coli bacteriophages. Analytical work is being carried out on several phages purified by these methods. Its results will subsequently be described in detail.

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The Combined Effect of Potassium Iodide and Streptomycin on Established Tuberculosis in Guinea Pigs

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It is a well-known clinical observation that iodides cause tubercle bacilli previously absent to appear in the sputum of patients with pulmonary tuberculosis. Jobling and Petersen (2) reported in 1914 that iodine will combine with the unsaturated fatty acids obtained from tubercle bacilli and will neutralize their ferment-inhibiting properties. Subsequent to this neutralization, ferment action ensues within areas of caseation with liberation of the bacilli and their appearance in the sputum. They also stated that iodine might serve another purpose by facilitating solution and absorption of the caseous matter, thus exposing the bacilli, which otherwise might be inaccessible to the influence of an effective therapeutic agent. In the light of this very significant work and in view of the

relatively poor results obtained in the treatment of fibrocaceous tuberculosis with streptomycin alone (1), it seemed highly desirable to test the combined effect of potassium iodide and streptomycin against established tuberculosis in guinea pigs.

First of all, it appeared essential to determine *in vitro* any possible effect of KI on the antibiotic potency of streptomycin. This was done by mixing varying concentrations of streptomycin with serial dilutions of potassium iodide ranging from .01 to 1.6 M concentration in infusion broth at 56° and 95° C for 7 min. The antibiotic titer of these mixtures was tested by using a fast-growing strain of tubercle bacillus. No alteration in the potency of the streptomycin was observed when compared with controls after incubation.

In view of these results, four groups of young guinea pigs, varying from 350 to 450 gm in weight, were inoculated in the groin with 1 cc of an aqueous suspension of tubercle bacilli (H37RV) containing 0.30 mg/cc. Seven pigs served as a control group; the other three groups (10 pigs each) were treated, respectively, with potassium iodide alone, with streptomycin alone, and with both streptomycin and potassium iodide. Treatment was begun 21 days after inoculation. The dosage of potassium iodide was calculated on the basis of 80 mg/kg of body weight/day and was given in a weak aqueous solution (16 mg/cc) by stomach tube once daily. The dosage of streptomycin was calculated on the basis of 12,500 µg/kg of body weight/day and was injected intramuscularly at 6-hr intervals. During the course of four weeks treatment, the inguinal nodes in the streptomycin-potassium iodide group remained significantly smaller than those in the other three groups. At the end of four weeks of treatment and the seventh week of infection, all animals were sacrificed and autopsied. On gross examination, the controls and KI guinea pigs showed heavy tuberculous infection of all the viscera, in the streptomycin group five pigs showed spread to the organs, whereas in the streptomycin-KI group the organs were entirely free from infection.

A subsequent survival experiment was run, using young pigs ranging from 350 to 450 gm in weight. This time three groups of guinea pigs were used: 15 in a control group, 15 in a group treated with streptomycin alone, and 16 in a group treated with both streptomycin and potassium iodide. Inoculation with H37RV was carried out in exactly the same manner as in the preceding experiment. Treatment was delayed, however, until the end of the fourth week of infection. The potassium iodide dosage was the same as that used in the first experiment. The streptomycin was increased to three times the former dosage. Treatment was carried on for a period of five weeks and then discontinued. At the end of the twelfth week of infection, 13 of the 15 in the control group were dead, 5 of the 15 in the streptomycin group were dead, and only 1 of the 16 in the streptomycin-KI group had succumbed. At this time two animals in each group were sacrificed and autopsied for the purpose of obtaining microscopic sections from the three groups simultaneously. Results of microscopic studies will be reported in a future communication. Excluding the two pigs sacrificed from

each group, the deaths from tuberculosis at the end of the 15th week of infection were: controls, 13 of 13 animals; the streptomycin group, 6 of 13; the streptomycin-KI group, 2 of 14. The respective mortality percentage rates were thus 100%, 46.1%, and 14.3%.

These results offer many interesting possibilities for further investigation. Clinical tests are now in progress.

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Graphite Bearings for Mechanical Stirrers

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Machined graphite bearings placed at strategic points in the mercury seal of a laboratory stirrer permit extremely rapid stirring with a minimum of attention. Graphite can be turned down on an ordinary lathe that is equipped with a chuck or collets. Precision tooling is not necessary. These bearings are machined in such a manner as to allow free movement of the bearing surfaces without permitting the stirrer shaft to wobble. Because of the variations in glass tubing sizes, it is found advantageous to tailor each set of bearings to fit the seal for which they are intended.

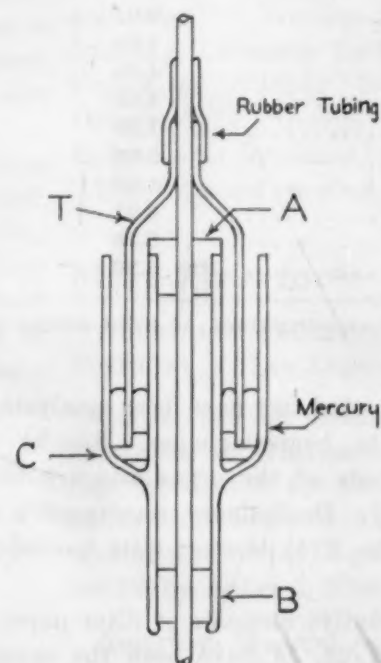


FIG. 1

The cross section of such an assembly (Fig. 1) shows a set of three bearings, which has been found to be the most stable arrangement. Bearings A and B furnish dual bearing surfaces between the stirrer shaft and the inner tube of the mercury seal. Bearing C braces the lower end of tube T, which rotates with the stirrer shaft. The lower end of the inner tube must be slightly constricted by fire polishing to prevent bearing B from fall-

ing out of the seal. The shoulder on bearing A holds it in the top of the inner tube. Bearings A and B are drilled and turned down on the lathe as a single unit and cut with a hack saw.

For ordinary stirring, bearing C can be eliminated. Its purpose is to steady the end of the rotating tube, T, and to check mercury splashing. Use of this bearing is suggested when especially stable setups are desired, very long stirring periods are required, or larger setups are used.

The use of ball bearings, suggested by Hershberg (1), facilitates rapid stirring, but the nature of the materials involved in most chemical reactions makes it impractical to install a set of ordinary steel ball bearings inside the seal or flask. The ball bearings must therefore be mounted quite far from the free end of the stirrer shaft. Greater stability can be obtained by supporting the shaft nearer the stirrer end by a graphite bearing such as B.

The problem of splashed mercury finding its way into the reaction vessel is virtually excluded by the presence of bearing A. Bearing B decreases the refluxing of solvents within the seal and makes subsequent cleaning of the seal a much easier task. Other advantages of the graphite bearings are: ease of assembly of the seal, durability, self-lubrication, and chemical inertness of the materials involved.

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Tissue Potassium Determinations¹

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A simple and relatively rapid method for determination of potassium concentrations of tissue has been developed in our laboratory.

From a series of ether-killed male albino rats of ca. 200-gm weight, brains and gastrocnemius muscles were removed and weighed. Tissues were then placed separately into 100 or 200 cc of distilled water and boiled under reflux condensers for 10 min. Solutions were stoppered and stored at 3° C for 36 hrs.

In the case of brain, sufficient agitation to fragment the tissues usually followed boiling, while in the case of muscle, a clear supernatant fluid was characteristically obtained.

At the end of 36 hrs aliquots taken from the supernatant liquid for potassium determination were analyzed by the flame photometer (Perkin-Elmer Model # 18); the boiled tissues, as a control of the method, were removed, dried at 105° C for 1-2 hrs, and then ashed in a muffle furnace at 550° C for 2 hrs. Tissue ashes were taken up in 0.1 N HCl, transferred through ash-free filter paper

¹ Aided by contract N6 ori-197 of the Office of Naval Research.

(S & S Blue Ribbon) to 50- or 100-cc volumetric flasks, and made up to volume with distilled water.

Analysis of the supernatant liquids of 23 brain and 17 muscle preparations yielded mean values of 3.42 ± 1.08 mg of K/gm of wet brain and 3.96 ± 0.12 mg of K/gm of wet muscle.

Application of Fisher's *t* test showed that there was no statistically significant difference between the standard errors of the mean potassium content values obtained by this method and the total potassium values determined by photometric analyses of a series of brain and muscle homogenates, P being 0.5 for brain and 0.4 for muscle.

Subsequent analysis of the tissue ash solutions described above, which were prepared at 2-4 times the concentrations of the solutions in which the tissues had been boiled, in a series of 20 experiments showed without exception that no more potassium remained in the boiled tissue than could be found in a corresponding volume of supernatant fluid. At the dilutions employed, this amount is negligible.

The method described above is recommended for total potassium analyses because, in addition to its simplicity and speed, it obviates the necessity of more arduous ashing or homogenizing techniques.

Duration of Viability of Neurotropic Viruses in an Experimental Plumbing System Contaminated by Back-Siphonage¹

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The possibility that poliomyelitis and other virus diseases may be spread by contaminated drinking water has been considered by many investigators. Various factors relating to the epidemiology of virus diseases have been studied. Laboratory experiments indicate that the poliomyelitis virus enters the body through the alimentary tract (5), and it has been shown that it is excreted in the stools of patients and persons not showing clinical evidence of the disease (11, 14). Furthermore, studies reveal that the poliomyelitis (6), St. Louis encephalitis, Japanese B (3, 15), and infectious hepatitis (4) viruses produce infection when given by mouth.

The poliomyelitis virus has been isolated from municipal sewage during epidemics in Europe and the United States (10, 12, 13, 17). The safety factor provided against bacteria through chlorination of water does not seem to apply to viruses. These studies and those carried

¹ These studies were supported by a grant from the American Society of Sanitary Engineering.

out by Kempf and Soule (7, 8) indicate that the amount of chlorine found in municipal drinking water is not enough to kill viruses of the neurotropic group.

In 1939 Kling (9) reported the isolation of a polio-like virus from well water in Sweden. The well was located on the premises where a child was afflicted with poliomyelitis. Aside from this report, however, we have been unable to find evidence of virus isolation from water.

Although the presence of virus has not been established in drinking water, the possibility that virus diseases may be transmitted by contaminated water should not be disregarded. The studies of Cronkright and Miller (1),

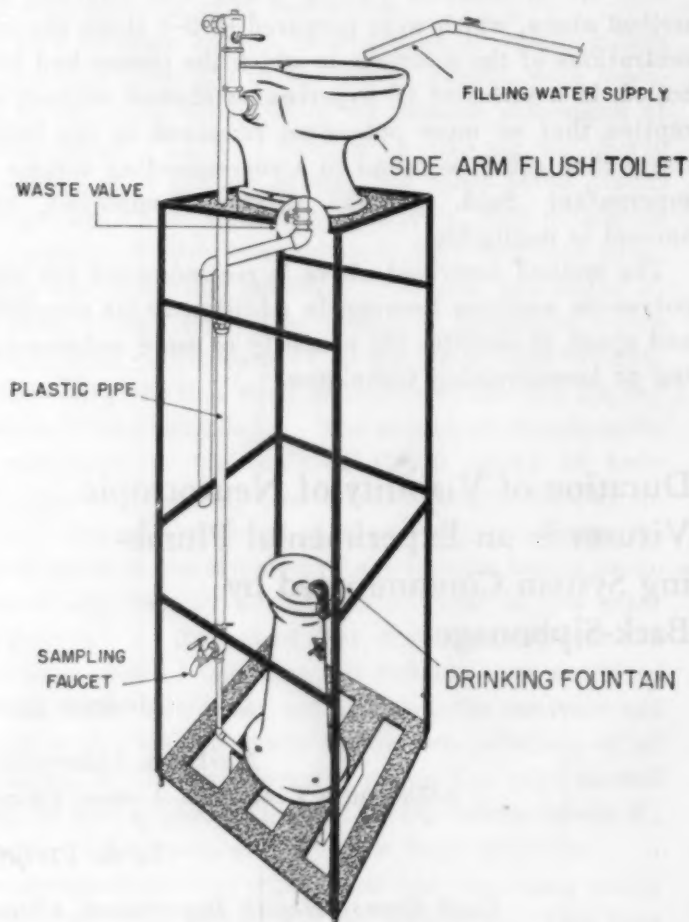


FIG. 1

Stockton (16), and Dawson and Kalinske (2) show that water supplies may be contaminated with sewage by many means of cross-connections and back-siphonage. Several factors may be responsible for the failure to isolate virus from water. Water in a plumbing system is continually changing, and by such a process the virus may be washed away or diluted so much in a relatively short time that its isolation could not be made. In addition, the methods of demonstrating the presence of virus are difficult, and in most cases the studies are made too late in the course of the epidemic.

Our studies were undertaken to determine if a plumbing system could be contaminated experimentally with neurotropic viruses by back-siphonage and to determine how long these viruses remained infectious when suspended in chlorinated drinking water and retained in the plumbing system.

The studies were made with the Western equine encephalomyelitis, St. Louis encephalitis, poliomyelitis (Lansing strain), and lymphocytic choriomeningitis viruses. The source of the virus in each case was infected mouse brains. Municipal drinking water containing about 0.1 ppm of chlorine was used for suspending the viruses. In each experiment the virus was diluted 1-5,000. A plumbing system representing that found in a two-story residence building was constructed for the study. The toilet bowl was of a flush valve type with a side-arm inlet. It was placed on a stand 9' above the floor, and a faucet and a drinking fountain were connected to it at floor level. All the parts used were of standard make. Fig. 1 shows the plumbing system.

The experiments were performed by filling the toilet bowl with water to the lower edge of the top rim. The descending pipe was also filled with water, and its upper end was closed. When the temperature of the water in the bowl attained that of the room, the virus was added to make a 1-5,000 dilution. The experiments were carried out at room temperature which ranged from 24 to 28° C. The siphon was started by opening either the faucet or the drinking fountain. This represented a simple form of back-siphonage, and with it, it was possible to draw the virus suspensions out of the bowl only to the level of the side outlet pipe.

Thirty minutes after the virus suspensions were drawn into the plumbing system by back-siphonage, 100 samples were obtained from both the faucet and the drinking fountain and tested for the presence of virus. Thereafter, samples were drawn from the faucet at 24-hour intervals to determine how long the viruses remained infectious when held in the plumbing system.

Since it was not practical to sterilize the entire plumbing system before the addition of the viruses, it was necessary to free each sample of bacterial contamination. Those containing the Western equine encephalomyelitis, lymphocytic choriomeningitis, and St. Louis encephalitis viruses were filtered through and N Berkefeld filter. The samples of poliomyelitis virus were treated with ether. Immediately after treatment the samples were cultured in thioglycollate media and then inoculated subcutaneously in Albino Swiss mice. The remainder of each sample was stored in dry ice, and, if bacterial contamination was found in any, the treatment was repeated and another set of animals was inoculated. In each experiment the presence of virus was established in the original virus suspensions and in the samples taken from the plumbing system.

The presence of the virus was established by inoculating from 6 to 12 mice with each sample. Each mouse was given 0.03 cc of the suspension by the subcutaneous route. Albino Swiss mice, each weighing about 12 gm, were used. After recovery of the virus from the plumbing system from the first sample taken, its identity was established by the neutralization test with specific serum. Three experiments were performed with each virus.

The results in Table 1 show that in each experiment

Role of Sulfhydryl Compounds in Pigmentation

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In recent studies (8) it was found that aqueous extracts of human epidermis inhibit the oxidation of *l*-tyrosine and *l*-dihydroxyphenylalanine (dopa), thus preventing the formation of melanin. Since this effect is counteracted by iodoacetamide, it has been assumed that the inhibition is due to the presence of sulfhydryl compounds in the extracts.

Further evidence in support of this assumption is submitted in this communication. The inhibitory principle is water soluble, dialyzable, and heat stable and is counteracted by *p*-chloromercuribenzoic acid and by cupric ions. Direct evidence is supplied by *in vitro* experiments demonstrating the relationship between the inhibitory activity of epidermal extracts and their sulfhydryl content. It is found that the degree of inhibition of melanin formation varies directly as the logarithm of the molar concentration of -SH.

A similar relationship is demonstrated *in vivo* following ultraviolet irradiation of the skin. In these experiments an increase in melanin formation is found to be preceded by a decrease in the -SH content of the skin. Immediately following exposure of the shaved skin of rabbits to large doses of ultraviolet light there is a decrease of from 24% to 83% in the concentration of -SH in the skin. This suggests that pigment-producing stimuli act by eliminating the -SH inhibition, allowing the enzymatic oxidation of pigment precursors to occur.

A clue as to the possible mechanism of this elimination is provided by another defense reaction of the tegument to ultraviolet irradiation and to other injurious stimuli, namely, an increased production of keratin, manifested as a thickening of the horny layer in man (7) and as excessive hair growth in animals (6). The production of keratin is characterized by the formation of disulfide (-S-S-) bridges from sulfhydryl groups of native proteins. Possibly the same biochemical process, the oxidation of sulfhydryl groups to disulfides, is responsible for both intensified keratinization and pigmentation.

Additional information concerning the role of sulfhydryl compounds in melanin formation is provided by two observations: first, that a copper-containing enzyme, tyrosinase, is apparently essential for the formation of melanin in mammalian tissues (2, 4, 5), as it is in plants and lower animal forms; and second, that sulfhydryl-containing epidermal extracts neutralize the effect of both tyrosinase and cupric ions in pigment production. Copper is known to be an essential dietary factor in the maintenance of the color of fur (3, 10). Moreover, our analyses have confirmed and extended earlier data (1, 9) which show that in most cases the black and gray hair of rabbits, guinea pigs, and rats contains significantly

¹ American Cancer Society Fellow, 1948-49.

TABLE 1

CONTAMINATION OF AN EXPERIMENTAL PLUMBING SYSTEM WITH NEUROTROPIC VIRUSES BY BACK-SIPHONAGE

Type of specimen	No. of experiments	Viruses employed				Ident. of virus
		L.C.M.	Polio (Lansing strain)	W.E.E.	St. Louis	
Original	3	15/15*	12/18	18/18	18/18	Pos.
From faucet	3	32/36	28/36	35/36	36/36	Pos.
From fountain	3	34/36	31/36	36/36	32/34	Pos.

* Mice dead/mice used.

The plumbing system for several days in each set of experiments. Survival time for the different viruses in experiments 1, 2, and 3, respectively, was as follows: lymphocytic choriomeningitis—7, 3, and 4 days; poliomyelitis (Lansing strain)—4, 1, and 2 days; Western equine encephalomyelitis—5, 2, and 4 days; and St. Louis encephalitis—4, 3, and 2 days.

These experiments show that a plumbing system may be contaminated with the neurotropic viruses studied by a simple form of back-siphonage. They also show that, when these viruses were suspended in chlorinated drinking water and retained in the plumbing system at room temperature, they remained infectious for several days.

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more copper than the white hair of the same animals. We have also found that among heavy metal ions, cupric ion has by far the strongest catalytic effect on the auto-oxidation of dopa. Expressed in molar concentration, cupric ion is 70 times more active than manganous and 100 times more active than ferrous ion.

The above observations suggest that within resting melanoblasts sulfhydryl compounds keep balance with a copper-containing enzyme, in analogy with *in vitro* experiments where epidermal extracts and cupric ions neutralize each other's effect on the substrate dopa. Under the action of pigment-producing stimuli, such as radiation, this equilibrium is disturbed by the oxidation of -SH groups, the enzyme thus being enabled to act freely on the substrate to form pigment.

Further evidence for a balance between enzyme and inhibitor is found in the more stable conditions of genetically induced pigmentation. In mottled rabbits white skin samples containing no enzyme, as shown by negative dopa reaction, yield from 25% to 44% lower -SH values than pigmented skin samples of the same animal.

Detailed experimental data will be presented elsewhere.

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Detection of Sulfur-containing Amino Acids on Paper Chromatograms¹

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The recent description, in a paper of Chargaff, *et al.* (1), of a method for the detection of cystine, cysteine, and methionine on paper chromatograms has prompted us to present a method employing potassium iodoplatinate as the reagent which we have used for similar purposes. Cystathionine, lanthionine, djenkolic acid, methionine sulfone and sulfoxide, cystine disulfoxide, and cysteine

¹ Aided by a grant from the Verna Hare Cancer Fund.

sulfonic acid, in addition to the first-mentioned amino acids, react with this compound. While, to our knowledge, it has not been used for chromatographic purposes, Sease and co-workers (4) have recently given a partial review of the literature on the reaction between organic sulfides and iodoplatinate and have described a quantitative procedure for analyzing organic sulfides and disulfides with iodoplatinate. Bleaching of the reagent by urine, albumin, tannic acid, gallic acid, pyrogallol, KCN, KCNS, and saliva, but not by urea, uric acid, starch, dextrin, sucrose, glycerol, gelatin, oxalic acid, tartaric acid, citric acid, carbon disulfide, and alcohol was apparently first described in 1881 (3).

The reagents used are 0.066 M KI and 0.0033 M H_2PtCl_6 . Mixing of equal volumes of these solutions yields a deep red solution, the color of which may be attributed to the ion $(PtI_4)^-$ (3). This reagent has been found stable for at least two weeks at room temperature. For spraying purposes, a 1:6 dilution has given the best compromise between contrast and sensitivity.

TABLE 1

Amino acid	R _F	Bleaching time	Amount detected (%)
Cystathionine	0.30	Immediate	24
Cysteine	*	2 min	12
Cysteine sulfonic acid	0.21	Immediate	12
Cystic acid	0.10	Does not bleach	..
Cystine	0.25	2 min	12
Cystine disulfoxide	0.21	Immediate	12
Djenkolic acid	0.30	"	12
Lanthionine	0.27	"	24
Methionine	0.76	"	12
Methionine sulfone	0.65	"	18
Methionine sulfoxide	0.81	"	18

* Cysteine could not be detected on the chromatogram when phenol was used as a solvent.

In practice, the completed chromatogram is dried as usual and then washed thoroughly in a 1:1 acetone-ether solution to remove traces of the chromatographing solvent. The paper is dried at 90° and sprayed evenly and lightly with the diluted reagent. Although all of the amino acids mentioned can be detected by bleaching areas against a pink background when tested on filter paper without chromatographing, on a finished chromatogram the reagent is usually bleached throughout the entire area. However, it has been found that suspending the sheet or strip, still damp from spraying, in a covered crock or cylinder containing a layer of concentrated hydrochloric acid on the bottom causes a redevelopment of the pink color by the HCl vapors, except in the areas occupied by the sulfur amino acids, which remain colorless. Air drying of the redeveloped sheet (heat will cause charring) yields a chromatogram on which the bleached areas are stable for many days. Eventually, bleaching of the entire sheet occurs. In the case of methionine sulfoxide and cystine disulfoxide, the bleached spots were faintly yellow, and the application of a starch solution revealed the presence of iodine. This was not

case with methionine sulfone or cysteine sulfinic acid or with the other amino acids tested. Bleached areas may be more readily observed by the transmitted light of an X-ray viewer.

R_f values (2) for the phenol-ammonia-gas system, together with a description of the rapidity and sensitivity of the test, are given in Table 1. The column describing amounts detectable denotes quantities which we have readily discerned. Sensitivity thresholds are probably much lower. On a nonchromatographed sheet methionine could be detected at a 0.4- γ level. Because of spreading during chromatographing, sensitivity is decreased.

Of the other amino acids ordinarily encountered, only leucine and serine affect the reagent at all. After 3 days these give only faint tests—not strong enough to be confused with the sulfur-containing amino acids. Except for cysteine acid, the reagent seems to be specific for the sulfur amino acids and is sensitive to the quantities commonly encountered in paper chromatography. It is rapid and convenient to apply and may be considered a useful adjunct to the many other methods rapidly becoming available for the detection and estimation of chromatographed material.

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Brain-Wave "Correlator"

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What is believed to be a new instrument for analyzing the electrical activity of the brain consists of two square-wave generators, actuated by the outputs of two channels of an electroencephalograph. Each square-wave crosses the axis at the same instant that its original EEG signal does, but is independent of the latter's wave-form and amplitude. Addition of these square-waves produces a voltage which is a three-valued function of time, being positive when both inputs are positive, zero when they are of unlike sign, and negative when both are negative.

The "voltage" of this composite square-wave, as read on a suitably lagged and calibrated a-c voltmeter, indicates the fraction of the total time during which the two inputs are of the same sign. If the inputs are alike, this fraction is unity and the meter reads +1. If one input is reversed, the fraction is zero and the meter reads -1. Unrelated inputs are of the same sign half of the time, and the reading is zero. Intermediate positions of the meter quantify the correlations reproducibly and more precisely than can be done by inspection.

Monopolar leads (the "indifferent" lead being placed on the ear lobe) have been used in observations on man. To date, only positive correlations have appeared between any two electrodes on the scalp; yet low values of correlation obtainable with certain locations of electrodes indicate that the common activity introduced by the ear is not of much consequence. High correlations sometimes occur when electrodes are symmetrically placed. Disturbing noises or hyperventilation reduce the correlation.

In cats and monkeys with exposed cortex, correlation increases with proximity of the electrodes, but it also depends on functional organization. With the two electrodes in one neuronographic area a high correlation is obtained, but this drops—sometimes abruptly—when one electrode crosses the border into another area.

In one cat Metrazol and one other convulsant each lowered the correlation, whereas CO_2 raised it.

These correlators are now in use in clinical electroencephalography and in experimental neurophysiology, but it is too soon to estimate their full utility.

Spontaneous Increase in Potency of Thromboplastin From Acetone-extracted Brain Tissue¹

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In the course of studies in our laboratory on the one-stage prothrombin test (Quick), a spontaneous increase was observed in the potency of thromboplastin prepared from an acetone-extracted (2) human brain specimen. Our methods for the preparation of reagents and for performing the prothrombin test are given in detail elsewhere (1). One feature of this procedure of significance in the present observations is the storage of large quantities of acetone-extracted brain in an evacuated calcium chloride desiccator in a refrigerator. We have found no significant change in the potency of thromboplastin prepared from brain tissue stored in this manner for periods up to two years, *provided the material is gradually used up during the period of storage*. However, we have found that unused remnants of brain tissue, stored in this manner, may exhibit striking increases in potency and other unusual characteristics.

The thromboplastin reagents used in these experiments were prepared by incubating 0.3 gm of acetone-extracted brain tissue in 5 cc of 0.9% NaCl solution for 15 min at 48°-50° C. The milky supernatant fluid was used for testing. Solutions of either 0.0075M or 0.025M CaCl_2 were used for recalcification. All dilutions of plasma and thromboplastin reagent were made with 0.9% NaCl.

A specimen consisting of several hundred grams of acetone-extracted human brain (H 46) showed no change in thromboplastic potency during a storage period of 210 days. A remnant consisting of 2.5 gm of this material, which was stored in a 50-cc Pyrex beaker, was

¹ Aided by a grant from the Christine Breon Fund.

not used again until the 257th day. However, the desiccator which contained it was opened daily. Additional prothrombin tests on normal plasma, using thromboplastin reagent prepared from this remnant, were made between the 257th and 701st days of storage.

TABLE 1*

Subject	Duration of storage of original specimen (days)	Duration of storage of remnant (days)	"Prothrombin time" (sec)		
			Concentration of plasma		
			100%	50%	12.5%
T. L.	210	0	10.1	12.3	32.6
J. L.	210	47	8.2	11.0	25.1
T. L.	210	65	8.0	10.2	22.2
N. F.	210	69	6.4	6.2	18.6
T. L.	210	491	4.6	2.7	17.7

* Progressive increase in potency of thromboplastin reagent prepared from remnant of acetone-extracted human brain specimen (H 46) stored *in vacuo*.

These tests showed a striking decrease in the "prothrombin time" of all plasma concentrations tested (Table 1). Furthermore, the "prothrombin time" of plasma diluted to 50% of its original concentration was shorter than that of the undiluted plasma. A solution of 0.0075M CaCl_2 was used for these tests.

TABLE 2*

Plasma concentration (%)	"Prothrombin time" in seconds	
	With 0.0075 M CaCl_2	With 0.025 M CaCl_2
100	4.6	6.4
80	3.7	5.5
60	2.6	4.7
50	2.7	...
40	3.1	5.6
20	12.2	16.8
12.5	17.7	...
10	25.8	35.3

* "Prothrombin time" of progressive dilutions of normal plasma tested with thromboplastin reagent prepared from remnant of acetone-extracted human brain (H 46) stored *in vacuo*.

Between the 694th and 701st days of storage, progressive dilutions of normal plasma were tested with thromboplastin reagent prepared from this remnant, using both 0.0075M and 0.025M CaCl_2 solutions (Table 2). In Fig. 1, the results obtained are contrasted with those observed using a thromboplastin reagent prepared from a human brain specimen (H 47) which had been stored in the usual manner and had shown no spontaneous increase in thromboplastic potency. The reagent prepared from the remnant showed a progressive shortening of the "prothrombin time" which reached its nadir in plasma concentrations between 50 and 60%. With further dilution of the plasma, the "prothrombin time" became progressively longer. However, the "prothrombin time" of the 40% plasma concentration continued to be shorter

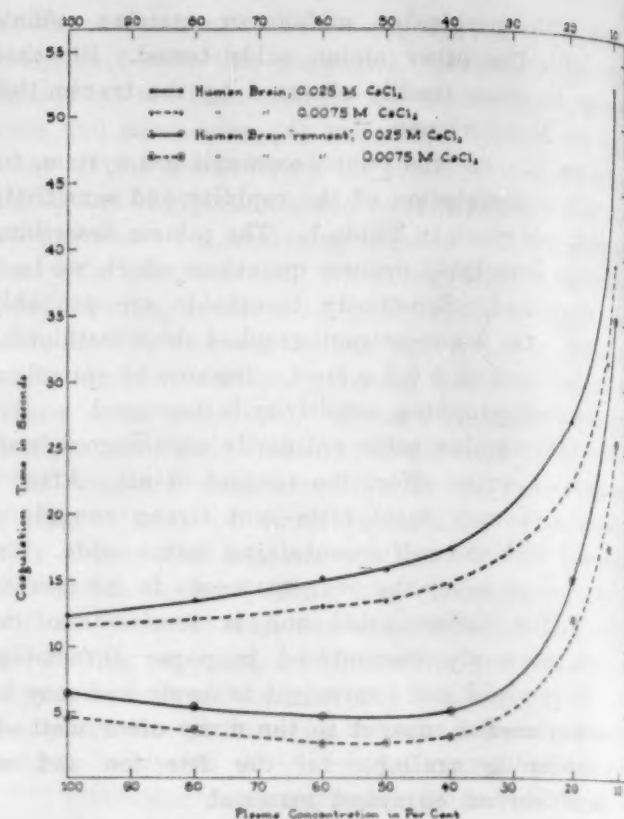


FIG. 1.—"Prothrombin time" of progressive dilutions of normal human plasma obtained with thromboplastin reagents prepared from standard acetone-extracted human brain specimen and its remnant.

than that of the undiluted plasma, and furthermore, this level there was found the greatest divergence from that prothrombin time obtained with thromboplastin reagent prepared in the usual manner.

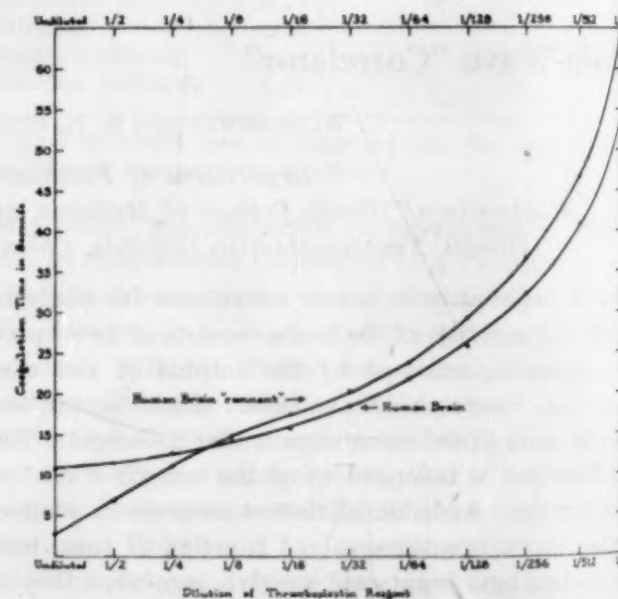


FIG. 2.—"Prothrombin time" of undiluted normal human plasma obtained with progressive half-dilutions of thromboplastin reagents prepared from standard acetone-extracted human brain specimen and its remnant.

On the 701st day of storage, progressive half-dilutions of thromboplastin reagent prepared from the last of remnant were tested with undiluted normal plasma using 0.025M CaCl_2 solution. The results are compared (Fig. 2) with a similar series of observations using a thromboplastin reagent prepared from a human brain in which no spontaneous increase in potency had occurred. For

Standardized Pain Stimulation as Controlled Stress in Physiological Studies of Psychoneurosis¹

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It is generally considered that the psychoneurotic is characterized by instability of various physiological systems and that this lability is particularly evident during stress. However, there is need for more specific information about the nature and extent of physiological changes which take place in the psychoneurotic patient under stress. It was considered that the experimental attack upon this problem would be greatly facilitated if a standardized situation of stress were available. This would permit comparisons to be made among individuals and among groups of patients, as well as between psychoneurotics and normals. The main requirements of a useful standard stress situation may be set forth as follows: (1) External stimulation should be uniform and controlled. (2) The stimulation should be relatively mild. Overstimulation may occur to the point where critical individual differences in reaction are obscured. Also, for practical reasons, a procedure to be used with psychiatric patients as subjects must not be frankly traumatic. (3) The stimulation, although relatively mild, should produce definite objective changes known to be associated with stressful experience. (4) Definite differences in test reaction should be detectable when individuals whose reactions differ clinically are exposed to the situation.

As a technique which appeared likely to satisfy these requirements, we selected a pain stimulation series presented by a Hardy-Wolff thermal stimulator (4) and carried out the present study to determine whether a series of pain stimuli of fixed order and intensity could be used as a standard stress situation. Since this procedure obviously satisfies the first two criteria, the investigation centered upon the remaining two, for which the technique seemed promising. Pain is generally associated with stress; and clinical observations suggest that the psychoneurotic overreacts to pain. The experimental work of Chapman (1), who used the Hardy-Wolff apparatus, has demonstrated differences between psychoneurotic patients and controls. Chapman has shown that the threshold for pain perception was almost exactly the same, but that patients reacted grossly to a degree of pain that was tolerated without reaction (head-withdrawal or wincing) by the controls. The present experiments were designed not for threshold-taking but for the presentation of a fixed series of standard intensities

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² The authors wish to acknowledge gratefully the advice and guidance of H. H. Jasper, of the Montreal Neurological Institute.

the data it is apparent that the increased thromboplastic potency disappears in a 1:8 dilution of the agent, and that on further dilution it becomes even less potent than that of the standard reagent. These results could be explained either by the removal of an anti-coagulant from the original brain specimen or by the formation of a coagulation accelerator other than thromboplastin in its remnant.

In order to confirm these observations a second specimen of acetone-extracted human brain (H 47), consisting of 400 gm of dried tissue, and a specimen of rabbit brain (R 47), consisting of 200 gm of dried tissue, were prepared. Aliquots, each consisting of 175 mg of tissue, were stored in Pyrex beakers in the same evacuated desiccator which contained the parent specimens. During ensuing 120 days thromboplastin reagents prepared from the parent specimens showed no change in potency, whereas those prepared from the aliquots exhibited an increase in potency similar to that observed with the

TABLE 3*

	"Prothrombin time" (sec)					
	Human brain (H 47)			Rabbit brain (R 47)		
	Concentration of plasma			Concentration of plasma		
	100%	50%	12.5%	100%	50%	12.5%
Original specimen stored for 120 days	11.7	15.0	35.7	12.3	16.6	40.9
Aliquot stored additional 120 days	7.7	6.7	22.9	5.7	4.5	17.0
Original specimen stored additional 120 days	11.8	15.4	36.8	12.5	16.7	40.8

* Spontaneous increase in potency of thromboplastin reagent prepared from small aliquots of acetone-extracted human and rabbit brains stored in *vacuo*.

remnant of tissue with which our original observations were made (Table 3). (Solutions of 0.025M CaCl₂ were used in these experiments.) However, other aliquots of human brain specimen (H 47) have so far shown no significant change in potency after 300 days of storage. That these changes were not due to further desiccation of the brain tissue was shown in the following manner: A portion of rabbit brain specimen (R 47) was found to have a moisture content of 2.4%. This was reduced to 1% by intense dehydration in *vacuo*. The dehydrated specimen showed no change in thromboplastic potency.²

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We wish to thank Walter E. Ward, of the Cutter Laboratories, Berkeley, California, for desiccating and determining moisture content of this sample.

to every subject, with measurement of physiological responses to stimulation as indices of reaction.

An objective indication of stressfulness is provided by the lymphocyte count, which has been shown to drop following certain forms of stress (3, 5, 7, 9). This involves activation of the anterior pituitary by the central nervous system, resulting in liberation of adrenocorticotrophic hormone. The consequent stimulation of the adrenal cortex leads to secretion of 11-17-oxysteroids, which promotes dissolution of the lymphocytes. Stress employed by former workers, viz., exposure to heat and pursuitmeter tests (6, 10), would seem to have been more strenuous and prolonged than the procedure employed in the present study. The lymphocyte study was made on a group of 10 patients, 8 psychoneurotics with anxiety, and 2 depressives.

As representative physiological measures serving as criteria of differentiation, records of finger movement and skin resistance, and electroencephalograms, were taken. These measurements were obtained during the pain test from a second group of 10 patients, selected so that most of the following characteristics were present: (1) conscious fears and anxiety—continuous, rather than intermittent, with depressed mood; (2) "poor control"—anxious manner, restlessness, some impairment to speech (stuttering, subdued tone of voice, unsteadiness of voice, tightening of throat); (3) increased "tension"—fatigue, increased tendon reflexes, and irritability; (4) tremor; (5) flushing; (6) palmar sweating; (7) anorexia; (8) insomnia. Absence of the following characteristics was required for selection: (1) anxiety which was specific to certain limited situations only; (2) obsessive-compulsive symptoms; (3) hysterical symptoms; (4) psychosis. These selective criteria served to bring together a group of patients whose anxiety level was high. Ten controls, who matched the patients in age and sex, were employed for purposes of comparison. These were taken from the medical and nursing staffs of the hospital. Anxiety level for this group, as a whole, would be expected to be considerably lower than that for the patient group.

The total period of examination, which lasted about 1 hr, was divided into three parts. During the first part the subject was reassured, given instructions, and prepared for the test (i.e. his forehead was blackened and electrodes were attached). A definite effort was made to reassure every subject about the relatively nontraumatic nature of the test. Details concerning the stimulation series were withheld, but the patient was assured that no electric shock would be administered.

Following this there was a 7-min rest period during which the subject was asked to relax. The test proper was then begun. During stimulation, light from a 500-watt lamp was focused on the forehead of the subject by means of a condensing lens. Stimuli were presented by means of an electronically controlled shutter which, when open, permitted light to pass to the subject's forehead.

Twelve stimuli were spaced at intervals of exactly 1½ min. All stimuli were 3 sec in duration, except the last stimulus, which lasted for only 1 sec. Intensities were varied by means of a Variac transformer which controlled

the voltage through the lamp. The intensity series, expressed in watts, was 500, 270, 340, 400, 270, 340, 270, 340, 400, 500, 500. The range of intensities for 3-sec stimuli was from approximately 0.23 gm cal/sec/cm² to approximately 0.44 gm cal/sec/cm². The most intense stimulus felt definitely painful to everyone.

During the test the subject sat leaning forward slightly with his chin in a rest. His left hand was strapped down (palm up) for skin-resistance recording, and his right forefinger rested on a button which he was instructed to press during stimulation when he thought that the heat on his forehead was about to become painful. The subject's eyes remained closed throughout the test.

During instructions the subject was informed that the forehead would be the place stimulated. He was told to expect a sensation of warmth, mounting into heat which might suddenly swell into a stab of pain. The subject was requested not to talk during the test, except when the examiner asked him a question. Exactly 30 sec following each stimulus the examiner asked the subject two questions: "How did that feel to you?" and "Did you press the button?"

The group of 10 patients whose lymphocyte counts were studied were fasted on the morning of the test, which was conducted in each case from 1:00 P.M. onward. Blood samples for white-cell count and differential were taken at 1:00, 3:00, and 5:00 P.M. Control lymphocyte counts also were made at the same times on the same subjects the day following this stress situation, when testing was being done.

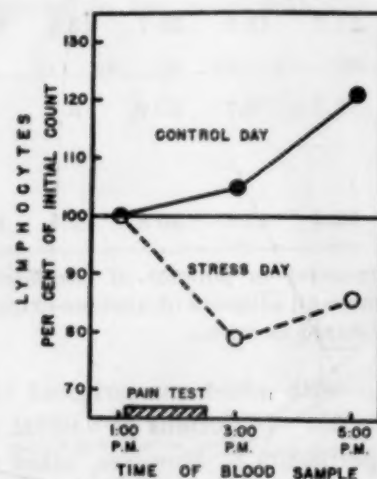


FIG. 1. Effect of pain test upon lymphocyte count.

The mean lymphocyte counts for the group on stress and control days are plotted in Fig. 1. The difference between these mean counts was reliable at the 3% level of confidence, both when the 3:00 P.M. and 5:00 P.M. counts were compared with the 1:00 P.M. count.

For the purpose of recording finger movements, a rugged Rochelle salt crystal was converted into a push-button pick-up, and the output of the crystal was fed into an amplifier of an Offner electroencephalograph. For purposes of analysis, we divided the record into four time segments: (1) during the 3-sec stimulation, (2) 3 sec immediately following stimulation, (3) 20 sec following the question, and (4) 40 sec preceding the next stimulus.

If during any of these intervals finger movement greatly exceeded the base-line level of oscillation, a plus rating was scored for that particular time segment. A plus rating was also made if the subject pressed the button voluntarily. Thus, it was possible to score 5 pluses for each of 12 stimuli and to grade all subjects on a scale from 0 to 60. Ratings were made by a technician from whom identity of the records was withheld in order to eliminate subjective bias.

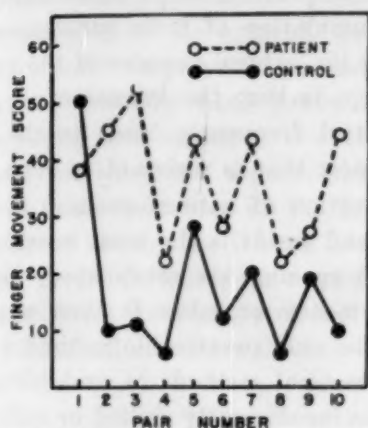


FIG. 2. Total finger movement scores for matched pairs; comparison of each patient with his matched control (maximum score = 60).

The finger movement data from the matched groups are presented in Fig. 2. The only reversal was that of control with a score of 50. This finding is of particular interest because, actually, it turned out not to be a reversal at all. Each subject was questioned at the conclusion of the test. The relevant part of this control's protocol reads as follows: (Question) "What was the most unpleasant experience which you have ever had?" (Answer) "I have experienced considerable anxiety. I had an acute anxiety state for about 3 years (about 6 years ago). I got over it with psychotherapy. The unpleasant feelings were feelings of panic and tension. I was so tense that noises (such as talking or the sound of door closing) actually hurt me; they were physically painful." In spite of this reversal, which was treated statistically as though it were a true reversal, the difference between patients and controls is reliable at the 1% level of confidence. Differences between groups were significant for each of the four separate time segments. The difference for the number of voluntary pressures on the button was not significant.

Analysis of skin-resistance records showed a higher frequency of anticipatory responses in the patient group. There was only one reversal (again the case of the control with the history of anxiety state); all of the other pairings showed a higher frequency of anticipatory responses for the patient member (see Fig. 3). One EEG lead (midline parieto-occipital) was employed. EEGs were analyzed by a modification of the Davis (2) technique for the variables per cent alpha, alpha frequency, fast frequency content, and for the presence of abnormalities (any waves of 6/sec or less). No significant differences between matched groups were found with respect to any of these variables.

The results of the investigation show that the standard

conditions of stimulation met the two basic requirements of a good experimental stress situation. The measures of finger movement and skin resistance demonstrated in clear-cut fashion the differences between normals and anxiety cases. The drop in lymphocyte count also indicates objectively that the stress of the situation produced far-reaching physiological effects of pituitary-adrenal cortex stimulation. The pain series is therefore a simple, easily controlled stressful situation by which differential physiological response may be studied.

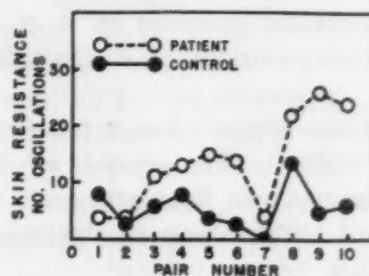


FIG. 3. Number of oscillations in galvanic skin response during anticipatory period; comparison of each patient with his matched control.

The finger movement recordings appear to be a particularly important indicator of motor disturbance associated with anxiety. Our findings in this regard are in accord with those of Luria (8), who conducted similar studies, although Luria's testing technique was designed more for analysis of disorganization of voluntary response. Our technique was such as to bring into focus the intrusion of "needless" muscle activity at times when no movement of the finger was required—that is, when the subject's finger was supposed to be at rest.

Luria relied almost exclusively upon measurements of finger movement in his studies of emotion. Our findings support his argument for the importance of motor disturbances in revealing general emotional disturbances. But it would seem desirable to conduct further research with more measures, tapping other physiological systems, such as the cardiovascular system, to obtain a broader picture of disturbances under stress and to provide the means for an objective comparison of reacting systems.

It appears likely that the pain series which was found to be useful in the present investigation may profitably be employed in more extensive analyses of disturbances in mental patients undergoing stress.

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Comments and Communications

Two New Organic Rhenium Compounds

Two new compounds not described in the literature have been prepared by reacting at room temperature potassium chlororhenite dissolved in 4 N hydrochloric acid with the hydrochlorides of diethylaniline and diethylamine.

The diethylaniline complex has a temperature of decomposition of 188° C. The crystals of this complex (dark green or microscopic light gray-green) are soluble in water and HCl but insoluble in absolute alcohol and in anhydrous ether.

The diethylamine complex has a temperature of decomposition of 210° C. The blue-green crystals of this complex are also soluble in water and in HCl but insoluble in absolute alcohol and in anhydrous ether.

$\text{ReCl}_4 \cdot [\text{C}_6\text{H}_5 \cdot \text{N}(\text{C}_2\text{H}_5)_2]_2 \cdot 2\text{HCl}$	contains	Re	N	Cl
		25.6	4.01	30.4
Found		27.0	4.04	30.7
$\text{ReCl}_4 \cdot [\text{C}_2\text{H}_5)_2 \cdot \text{NH}]_2 \cdot 2\text{HCl}$		34.0	5.12	38.9
Found		34.4	5.16	38.7

Evidently the two compounds have the compositions indicated.

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University of Alabama

Statement Recommending the Establishment of an International Biological Control Organization

The following statement from P. Vayssiere, secretary-general of the International Union of Biological Sciences, has been transmitted to us by Stuart Mudd, of the University of Pennsylvania, secretary of the Union:

The entomologists, representing 10 nations, gathered at Stockholm for the purpose of a symposium on the scientific basis of an international organization for biological control, knowing that the promotion of world peace, international understanding, and the welfare of peoples is the aim of UNESCO and AFO, bring to the attention of these powerful international organizations the opportunity and urgent need to achieve this aim, in part, by providing facilities for the development of basic research on biological control which will lead to the greatly extended use of natural enemies to control insect pests and noxious weeds, so helping to conserve world food resources.

To strengthen this resolution, the members of the symposium draw attention to the following important considerations:

(1) A great loss of human food is caused by the depredations of insect pests and the competition of

weeds. To ease the world shortage of food every effort must be made to reduce this loss to the lowest possible level.

(2) The use of insecticides has proved a powerful means of reducing loss. However, this method involves the continual expenditure of money and labor, and it has proved too expensive for use against the pests of many crops. Moreover, it is sometimes dangerous to man and domestic animals; and it may also directly damage the crops it is used to protect, or do so indirectly either by causing the accumulation of toxic substances in the soil or by destroying the natural enemies of the pests. A further disadvantage is that the intensive use of chemical methods of control frequently leads to the selection of a strain of the pest that is resistant to such control.

(3) The utilization of natural enemies for the control of insect pests and weeds is the most economical method once the natural enemies are established, for no further expenditure of money or labor is then required. Furthermore, it is the only practicable method when the cost of control by chemical methods is prohibitive and when available labor is insufficiently skilled or reliable to apply insecticides.

(4) It is clear that natural enemies could be used much more widely than they are at present, even though it is admitted that biological control cannot take the place of insecticides or herbicides for the control of every insect pest and weed. However, in their efforts to extend the field of biological control, entomologists are handicapped by their meager knowledge of the important natural enemies that exist in various parts of the world.

(5) To secure the necessary additional information, some form of international organization is essential, for the biological control of insect pests and weeds in any one region is effected by introducing natural enemies from other regions. Consequently the information required by any one country can be obtained only by research in other countries; and therefore such research must necessarily be handicapped if organized on a national basis.

To deal with the situation outlined above, international action can and should begin at once, by setting up an organization providing the following services: (1) a documentation service for the collection of pertinent information from all possible sources, and its dissemination to all interested organizations and individuals; (2) a taxonomic service to deal with the identification of natural enemies; (3) a survey service to study the natural enemies existing in the major regions of interest; and (4) an application service, devoted to collecting, breeding, transporting, and acclimatizing natural enemies and establishing these in regions where the nations concerned are unable to undertake this work themselves.

It is considered that the personnel of the taxonomic service should be stationed at existing major centers of taxonomic investigations and that the documentation service should be associated with one of these groups of taxonomists. For the survey service, groups of investigators should be stationed at appropriate centers, where

Special laboratory facilities will need to be provided. The formation of the application service should not be undertaken until the rest of the organization has been established.

The keystone of the proposed organization is the taxonomic service. Because of the dearth of competent taxonomists it will not be possible to staff it adequately until more young men are persuaded to undertake such work. To attract them, permanent posts carrying adequate remuneration must be created, and, in addition, the organization must be prepared to undertake the cost of the specialized training (and probably the training itself) of the young men selected.

The proposed international organization is viewed as an extension to other countries of the kind of work already being carried out by the United States of America and the British Commonwealth, the organization working in cooperation with all institutes and individuals actively carrying out biological control work.

Action Potentials From Single Auditory-Nerve Fibers?¹

We have in two published communications (*J. Neurophysiol.*, 1943, 6, 39-58; 1944, 7, 287-304) stated, directly or by implication, the following propositions:

(1) It is possible to isolate action potentials from single auditory-nerve fibers of the cat by using microelectrodes.

(2) Inhibition of activity in these fibers, produced by acoustic stimuli, occurs through a neural mechanism which does not include a synapse, i.e. one which presumably acts at the level of the hair cell in the cochlea.

Throughout our experiments on the cat nerve we were disturbed by the difficulty experienced in isolating the response of one fiber in a bundle of thousands of them; on occasion as much as a half-day of careful, continuous probing with the electrode was required before a successful position could be obtained (see *J. Neurophysiol.*, 1943, 6, 41). On the other hand, a contact once established was unexpectedly easy to maintain despite minor mechanical disturbances of electrode or preparation.

We can now supply a piece of important elementary information, inexcusably omitted from our earlier study, which bears upon these problems. We have recently examined the auditory nerve of the cat microscopically, in sections kindly provided by Dr. M. H. Lurie.

The auditory nerve in the stretch from the internal acoustic meatus to the medulla contains nerve cell bodies. These cell bodies are present throughout the region into which our microelectrode was ordinarily placed. They vary considerably in number but may amount to as many as 45 per high power field (about 0.1 mm²). Standard anatomical works thus far consulted do not describe these peripheral ganglion cells; they probably belong to the cochlear nucleus and are therefore second-order neurons in the auditory tract, although this has not been established with certainty.

This research was carried out under contract with the U. S. Navy, Office of Naval Research (Contract N5ori-76, Project NR147-201, Report PNR-61).

the auditory tract, although this has not been established with certainty.

There is, therefore, very good reason to believe that most, if not all, the potentials we have described were derived not from the auditory nerve but rather from cell bodies of second-order neurons. If this indeed be true, both of the propositions at the head of this note are incorrect. The first of them needs no further comment. The second, which deals with a peripheral inhibitory mechanism, will probably be discarded gladly by most neurophysiologists. If the potentials were obtained postsynaptically, the observation of inhibition of second-order neurons is interesting but not surprising.

All of our description of single-unit activity in the auditory pathway remains unchanged. The interpretations must be altered, however, to the extent to which we recorded the activity of second-order instead of first-order neurons.

We wish to acknowledge the gentle obstinacy of Dr. H. K. Hartline, who originally suggested we look for ganglion cells in the nerve, and who has never let the matter rest.

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On Obtaining Books From Germany

Dr. Julian Huxley writes:

"Students of biological evolution will, I think, be interested to hear something about the new book by Dr. Bernhard Rensch, *Neue Probleme der Abstammungslehre*, published by Ferdinand Enke Verlag (Stuttgart, 1947), which I have recently received and read.

"It appears to me to be a most valuable work, which treats of the method, and especially the course, of evolution in a comprehensive way. Its most original feature is the number of tables it contains, giving quantitative expression to various rules of evolution. It is also interesting in that the author, though working in complete isolation during the war, has arrived at conclusions in general similar to those reached by American and British specialists in the subject during the same period.

"It may be also useful to set forth the methods by which this, and other German books, may now be obtained. Anyone wishing to purchase books published in Germany may do so by placing his order through any bookseller, who may then apply directly to the publisher in Germany. The transaction is administered through the Joint Export and Import Agency of Military Government, and payment can be made in the currency of the country in which the original order is placed. The delay in obtaining the book may be a matter of some weeks or, of course, considerably longer if the publisher has not previously obtained a license for export from the Joint Export and Import Agency. However, many publishers who foresee a demand outside Germany for a particular book will have obtained the required license soon after the appearance of the book in Germany."

Genetic and Endocrine Determinants of the Plasma Urate Level

At the meeting of the American Rheumatism Association at Chicago in June 1948, Smyth, Cotterman, and Freyberg (*J. clin. Invest.*, in press) reported results of their investigation of genetic factors in gout and hyperuricemia. The discussion which followed indicated that quite similar conclusions had been reached independently by Stecher, Hersh, and Solomon (*Ann. int. Med.*, in press) at Cleveland City Hospital, and by Wolfson, Cohn, Levine, Hunt, and Rosenberg (manuscript in preparation) at Michael Reese Hospital. After mutual discussion it was agreed that the significance of the findings for normal and pathological physiology warranted a brief cooperative statement summarizing the essential results. The chief conclusions reached were:

(1) Asymptomatic hyperuricemia is a frequent finding in the relatives of patients with gout. Statistical analyses indicate that a single gene is probably responsible for the transmission of asymptomatic hyperuricemia; that this gene is dominant rather than recessive; and that the responsible gene is autosomal rather than sex-linked.

(2) Earlier reports (B. M. Jacobson. *Ann. int. Med.*, 1938, 11, 1277; K. Brøchner-Mortensen. *Acta Med. Scand.* (Suppl. 84), 1937, 1; H. A. Bulger and H. E. Johns. *J. biol. Chem.*, 1941, 140, 427) of a higher average normal plasma urate concentration in males than in females are confirmed. The mean reported ratio of average female plasma urate/average male plasma urate in 5 investigations has been 0.85 (Stecher, *et al.*; Wolfson, *et al.*; Jacobson; Brøchner-Mortensen; and Bulger and Johns). The values of this ratio, as found in individual studies, lie between a minimum of 0.80, reported by Bulger and Johns, and a maximum of 0.92, reported by Stecher, Hersh, and Solomon.

(3) The average plasma urate concentration is higher in gouty males than in gouty females (Wolfson, *et al.*). The average plasma urate in males who inherit asymptomatic hyperuricemia is higher than that in females who inherit asymptomatic hyperuricemia (Stecher, *et al.* and Wolfson, *et al.*). The average plasma urate is higher in those male relatives of gout patients who have not inherited hyperuricemia than in the corresponding group of female relatives.

(4) Since a sex differential in plasma urate levels occurs in normal adults, in patients with clinical gout, and in relatives of gout patients who inherit asymptomatic hyperuricemia, this sex differential or its underlying endocrine background cannot alone be the cause of gouty hyperuricemia. Similarly, the sex differential cannot be the sole mechanism through which the gene for hyperuricemia operates.

(5) Males who inherit asymptomatic hyperuricemia do not, as a rule, develop abnormally elevated plasma urate levels (above 6.0 mg%) until after puberty (Smyth, *et al.*). Female carriers of genetic hyperuricemia do not usually develop abnormally elevated plasma urate levels

until just before, or after, the menopause (Stecher, *et al.*). These findings suggest that the presence of male sex hormones unantagonized by female sex hormones provides an endocrine situation in which the gene controlling inherited hyperuricemia becomes activated to play its maximum effectiveness in producing an elevation of plasma urate level (Smyth, *et al.* and Stecher, *et al.*).

(6) Abnormally elevated plasma urate levels are more common in male relatives of the gouty than in female relatives. Statistical analysis indicates that this probably does not mean that more males than females inherit the gene for hyperuricemia. Rather, the difference in the incidence of abnormally high levels appears to depend upon two nonhereditary factors: (a) the fact that male carriers develop their maximum urate levels at an earlier age than female carriers, and (b) the existence of a normal sex differential in urate concentration.

(7) The data suggest a correlation between the duration and magnitude of hyperuricemia and the occurrence of clinical gout. The results are consistent with the view that clinical gout develops more frequently in males who inherit hyperuricemia because of three factors: (a) the plasma urate concentration of males is normally greater than that of females; (b) the gene responsible for the inheritance of hyperuricemia appears to be somewhat more effective in regard to the actual quantitative magnitude of elevation of the plasma urate level in males; and (c) since males who inherit hyperuricemia develop their maximal urate levels considerably before female carriers, this increased duration of hyperuricemia exposes the males to a proportionately increased risk of developing clinical symptoms. (The observation that the occurrence of clinical gout and the duration and magnitude of hyperuricemia are positively correlated should not be taken to mean that hyperuricemia is necessarily a direct cause of the symptoms of clinical gout.)

(8) Information is as yet incomplete in regard to the alteration in metabolism through which the gene for hyperuricemia produces an elevated plasma urate concentration and, similarly, as to the exact biochemical mechanism by which the normal sex differential in plasma urate level is maintained. Preliminary results suggest that the sex differential is associated with a reduction in males of the ratio of urate clearance/glomerular filtration rate. In turn, the reduction of this ratio seems to depend upon a tendency for urate clearance to be somewhat smaller in males than in females and for glomerular filtration rate to be somewhat greater in males than in females, when these values are expressed per unit of calculated surface area. However, in order to excrete this amount of urate the male requires a higher plasma urate than the female because of his smaller ratio of urate clearance to glomerular filtration rates. *Genetic hyperuricemia*, when studied at the time of onset of clinical gout, and provided male gout patients are compared with male control subjects, appears to be associated with an approximately equal reduction in urate clearance and glomerular filtration rate. The available data suggest that this decrease in glomerular

filtration rate, and presumably in urate clearance as well, occurs predominantly in the first two decades after birth, following which the rate of decline in function appears to be slowed. The major decrease in these renal functions thus appears to occur in a period which approximately coincides with the period during which the male carriers of inherited hyperuricemia develop elevated plasma urate levels. Such findings suggest that the decrease in glomerular filtration rate, which is a usual observation in the gouty, may in fact be largely genetically determined, rather than a complication of gout, as is usually assumed (Wolfson, et al.).

(9) It is suggested that normal standards for the upper limits of plasma urate concentration be revised to take cognizance of the normal sex differential in plasma urate level.

The complete data on which the foregoing statements are based will be published in detail elsewhere.

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Book Reviews

Atomic energy: being the Norman Wait Harris lectures delivered at Northwestern University. Karl K. Darrow. New York: John Wiley; London: Chapman & Hall, 1948. Pp. 80. (Illustrated.) \$2.00.

This brief absorbing treatment of the physics of nuclear energy retains the informal language of Dr. Darrow's lectures at Northwestern University. It is a contribution to the growing list of publications whose admirable objective is to explain the physics of nuclear energy to the layman and to scientists in other fields. Within its 80 pages the reader who seeks to obtain a general review of the field will find a surprising amount of sound information woven into an interesting story.

Starting with introductory information about the atomic structure of matter and an ingenious explanation of physical units in everyday language, the story proceeds with the aid of simple but effective diagrams to a brief description of nuclear forces and a careful cataloguing of the masses of simple nuclei. This leads to the apparent contradiction that in nuclear physics the whole is not equal to the sum of its parts, a problem which is solved by the explanation of the equivalence of mass and energy and a statement of Einstein's equation.

Following a more detailed discussion of energy units, the specific nature of nuclear forces and the inappropriate use of the term "atom smashing," the possibility of transmutation is examined and found to require giant machines of which the Van de Graaf generator is described as a typical case. With the aid of cloud chamber photographs, simple transmutations are explained and the verification of Einstein's equation noted.

A brief eulogy of Rutherford's phenomenal contributions leads to a discussion of the stability of heavy nuclei, radioactivity, and the peculiar advantages of the neutron as an atomic projectile. The discovery of atomic fission with its excess production of neutrons leads to the awesome implications of the chain reaction with its disturbing questions about the stability of our immediate surroundings. These are allayed with an explanation of the process provided by nature and the story ends with the removal of such brakes one by one to yield, on one

hand, the uncontrolled reaction or bomb and, on the other, the controlled reaction or pile with its singularly appropriate name. The story ends on the hopeful note that the controlled reaction can aid humanity in many ways if man can avoid further use of the uncontrolled reaction.

Dr. Darrow's book is distinguished among its kind by its brevity and the clarity of presentation. He gives enough, but just enough, information for the nonscientist to follow the essential ideas without becoming lost in extraneous details.

R. D. HUNTOON

National Bureau of Standards

Hemostatic agents: with particular reference to thrombin, fibrinogen and absorbable cellulose. Walter H. Seegers and Elwood A. Sharp. Springfield, Ill.: Charles C. Thomas, 1948. Pp. xii+131. (Illustrated.) \$4.50.

Recent rapid developments in the field of blood clotting have made available for the first time highly potent agents for stopping hemorrhage and bleeding. These substances have many possible applications. Associated with this development are important points of technique, descriptions of which are scattered through the literature or have not been published. Hence, there is a definite need for a simple description of these materials and their uses. This small book appears to meet this need admirably. The authors have been actively identified with many of the developments in this field.

The substances described are: thrombin, fibrinogen, oxidized cellulose, fibrin foam, and gelatin sponge. The chemical and biological properties of each substance are discussed, followed by a review of clinical uses found to date. In an introductory chapter the current views on the clotting of blood are sufficiently presented to give an understanding of the basis for the techniques described and their application. Evidently the authors have purposely avoided recent theoretical complexities in favor of providing information of immediate practical use.

This book will be of greatest value to those with surgical interests, with its immediate applications to neurosurgery, plastic surgery, gastroenterology, rhinology, urol-

ogy, and dentistry. As a summary of recent work which has transformed theoretical terms in textbooks of biochemistry and physiology to powerful tools in the hands of the clinician, it will be of interest to medical scientists generally.

L. B. JAQUES

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Scientific Book Register

- ADAMS, ROGER. (Ed.-in-Chief.) *Organic reactions*. (Vol. IV.) New York: John Wiley; London: Chapman & Hall, 1948. Pp. viii + 428. (Illustrated.) \$6.00.
- BATCHELOR, LEON DEXTER, and WEBBER, HERBERT JOHN. *The citrus industry*. Vol. II: *Production of the crop*. • Berkeley-Los Angeles: Univ. California Press, 1948. Pp. xv + 933. (Illustrated.) \$10.00.
- BAWN, C. E. H. *The chemistry of high polymers*. New York: Interscience, 1948. Pp. x + 249. (Illustrated.) \$4.50.
- BENBROOK, EDWARD A., and SLOSS, MARGARET W. *Veterinary clinical parasitology*. Ames, Ia.: Iowa State College Press, 1948. Pp. 187. (Illustrated.) \$4.50.
- BLACK, NEWTON HENRY. *An introductory course in college physics*. (3rd ed.) New York: Macmillan, 1948. Pp. xiv + 800. (Illustrated.) \$5.00.
- CLAUSEN, JENS, KECK, DAVID D., and HIESEY, WILLIAM M. *Experimental studies on the nature of species*. III: *Environmental responses of climatic races of Achillea*. (Publ. No. 581.) Washington, D. C.: Carnegie Institution, 1948. Pp. iii + 129. (Illustrated.) \$2.50 paper; \$3.00 cloth.
- COX, JOSEPH F., and JACKSON, LYMAN E. *Crop management and soil conservation*. (2nd ed.) New York: John Wiley; London: Chapman & Hall, 1948. Pp. xxii + 572. (Illustrated.) \$3.80.
- DAHLBERG, GUNNAR. *Mathematical methods for population genetics*. Basle, Switzerland: S. Karger; London: New York: Interscience, 1948. Pp. viii + 182. (Illustrated.) \$4.50.
- DEGERING, ED. F., and collaborators. *Fundamental organic chemistry*. Ypsilanti, Mich.: University Lithoprinters, 1948. Pp. xvi + 516. (Illustrated.)
- EBERSON, FREDERICK. *Microbes militant: a challenge to man*. (A revision of *The microbe's challenge*.) New York: Ronald Press, 1948. Pp. x + 401. (Illustrated.) \$4.50.
- JONES, FREDERIC WOOD. *Hallmarks of mankind*. Baltimore: Williams & Wilkins, 1948. Pp. vi + 86. (Illustrated.) \$2.50.
- KENT, GEORGE C. *Practical anatomy of the dogfish, *Necurus*, and cat*. Dubuque, Ia.: Wm. C. Brown Co., 1948. Pp. iii + 84. (Illustrated.) \$3.00.
- KLEINER, ISRAEL S. *Human biochemistry*. (2nd ed.) St. Louis: C. V. Mosby, 1948. Pp. 649. (Illustrated.) \$7.00.

- LIVINGSTON, ROBERT. *Physicochemical experiments*. (2nd ed.) New York: Macmillan, 1948. Pp. xiii + 393. (Illustrated.) \$3.50.
- MOTT, N. F., and SNEDDON, I. N. *Wave mechanics and its applications*. Oxford, Engl.: Clarendon Press; New York: Oxford Univ. Press, 1948. Pp. xii + 393. (Illustrated.) \$10.00.
- RASHEVSKY, N. *Mathematical biophysics*. (Rev. ed.) Chicago: Univ. Chicago Press, 1948. Pp. xxiii + 393. (Illustrated.) \$7.50.
- ROSS, HERBERT H. *A textbook of entomology*. New York: John Wiley; London: Chapman & Hall, 1948. Pp. ix + 532. (Illustrated.) \$6.00.
- SMITH, AUSTIN. *The drugs you use* (with a Foreword by Morris Fishbein). New York: Revere, 1948. Pp. xii + 243. \$3.00.
- STRUICK, DIRK J. *A concise history of mathematics*. Vol. II: *The seventeenth century—the nineteenth century*. New York: Dover Publications, 1948. Pp. 299. (Illustrated.) \$3.00.
- WILKS, S. S. *Elementary statistical analysis*. Princeton, N. J.: Princeton Univ. Press, 1948. Pp. xi + 393. \$2.50.
- . *The Royal Society Empire Scientific Conference, June–July 1946*. (2 vols.) Edinburgh, Scotland: Morrison & Gibb, Ltd., 1948. Vol. I: Pp. 828; Vol. II: Pp. 707. (Illustrated.) 2: 2: 0 net.
- . *Survey of food and nutrition research in the United States: 1947*. (Compiled by the Committee on Survey of Food and Nutrition Research, Food and Nutrition Board, with the support of the Committee on Food Research, Quartermaster Food and Container Institute for the Armed Forces.) Washington, D. C.: National Research Council, 1948. Pp. x + 306. \$1.00.

Just Received—

- ASMOUS, VLADIMIR C. *Fontes historiae botanicae sicae*. (Chronica Botanica, Vol. II, No. 2.) Cambridge, Mass.: Chronica Botanica, 1947. Pp. 87 + 125. (Illustrated.) \$1.25.
- BERNHARD, HUBERT J., BENNETT, DOROTHY A., and HUGH S. *New handbook of the heavens*. (2nd ed.) New York-Toronto: Whittlesey House, 1948. Pp. 360. (Illustrated.) \$3.00.
- KAGAN, SOLOMON R. *Fielding H. Garrison: a biography*. Boston: Medico-Historical Press, 1948. Pp. 104. (Illustrated.) \$4.00.
- MARTIN, L. C. *Technical optics: a revised and enlarged edition of "An introduction to applied optics."* (I.) New York-Chicago: Pitman, 1948. Pp. vii + 393. (Illustrated.) \$7.50.
- SMART, JOHN (with chapters by Karl Jordan and Whittick). *A handbook for the identification of insects of medical importance*. (2nd ed.) London: British Museum of Natural History, 1948. Pp. 295. (Illustrated.) 20/-.
- TRACEY, M. V. *Proteins and life*. London: Pilot Press, 1948. Pp. x + 154. (Illustrated.) 10/6.